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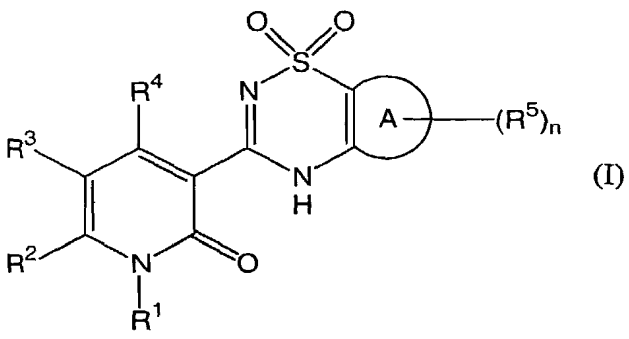
(54) Title: ANTI-INFECTIVE AGENTS



(I)

(57) Abstract: The present invention provides an HCV polymerase inhibiting compound having the formula (I) and a composition comprising a therapeutically effective amount of said compound. The present invention also provides a method for inhibiting hepatitis C virus (HCV) polymerase, a method for inhibiting HCV viral replication, and a method for treating or preventing HCV infection. Processes for making said compounds, and synthetic intermediates employed in said processes, are also provided.

ANTI-INFECTIVE AGENTS

Technical Field

The present invention provides novel anti-infective agents. Specifically, the present invention provides an HCV polymerase inhibiting compound, and a composition comprising a therapeutically effective amount of said compound. The present invention also provides a method for inhibiting hepatitis C virus (HCV) polymerase, a method for inhibiting HCV viral replication, and a method for treating or preventing HCV infection. Processes for making said compounds, and synthetic intermediates employed in said processes, are also provided.

Background of the Invention

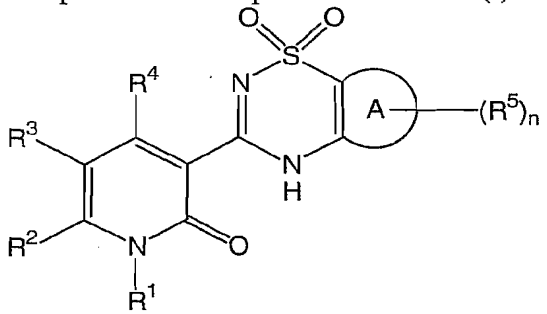
Infection with hepatitis C virus (HCV) is a major cause of human liver disease throughout the world. More than 85% of all infected individuals become chronically infected. Chronic HCV infection accounts for 30% of all cirrhosis, end-stage liver disease, and liver cancer in the United States. The CDC estimates that the number of deaths due to HCV will increase to 38,000/year by the year 2010.

While initially therapy consisted of interferon alone, the combination of interferon alpha-2b with ribavirin for either 24 or 48 weeks is currently the most efficacious approved therapy for the treatment of chronic HCV infection. However, there are many adverse side effects associated with this therapy (flu-like symptoms, leukopenia, thrombocytopenia, and depression from interferon, as well as anemia induced by ribavirin). Furthermore, this therapy is less effective against infections caused by HCV genotype 1 which constitutes about 75% of all HCV infections.

Based on the foregoing, there exists a significant need to identify compounds with the ability to inhibit HCV. The present invention provides novel anti-infective agents which are HCV polymerase inhibitors.

Summary of the Invention

The present invention provides a compound of formula (I)



(I)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

A is a monocyclic or bicyclic ring selected from the group consisting of aryl, cycloalkyl, cycloalkenyl, heteroaryl and heterocycle;

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bNalkyl$-, $R_aR_bNC(O)alkyl$-, $R_aR_bNC(O)Oalkyl$-, $R_aR_bNC(O)NR_calkyl$-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, -$N(R_a)(R_b)$, $R_aR_bNC(O)$-, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$ and $R_aC(O)$-; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$;

alternatively, R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is independently substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, -NH_2, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-,

$R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$, -$alkylC(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3

substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -alkyl$N(R_e)C(O)OR_f$, -alkyl$N(R_e)SO_2NR_fR_h$, and -alkyl$N(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)$N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkyl$N(alkyl)_2$, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)$N(alkyl)_2$;

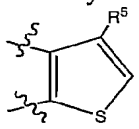
R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl,

cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bN$alkyl-, $R_aO$alkyl-, $R_aR_bNC(O)$-, $R_aR_bNC(O)$alkyl, R_aS-, $R_aS(O)$-, R_aSO_2-, R_aSalkyl-, $R_a(O)$Salkyl-, $R_aSO_2$alkyl-, $R_aOC(O)$-, $R_aOC(O)$alkyl-, $R_aC(O)$-, $R_aC(O)$alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

m is 0, 1, 2, 3, or 4; and

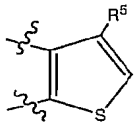
n is 0, 1, 2, 3, or 4;

with the proviso that when A is a monocyclic ring other than



and R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl;

and with the further proviso that when A is



and R^4 is hydroxy or R_eS-, and R^5 is hydrogen, unsubstituted alkyl, halo or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

The present invention also provides the processes of making a compound of the present invention and intermediates employed in the processes.

The present invention further provides a pharmaceutical composition comprising a therapeutically effective amount of the compound or combination of compounds of the present invention or a pharmaceutically acceptable salt form thereof, and a pharmaceutically

acceptable carrier.

The present invention also provides a method of treating or preventing infection caused by an RNA-containing virus comprising administering to a patient in need of such treatment the pharmaceutical composition of the present invention.

The present invention still further provides a method of inhibiting the replication of an RNA-containing virus comprising contacting said virus with a therapeuctially effective amount of a compound or combination of compounds of the present invention or a pharmaceutically acceptable salt thereof.

The present invention yet further provides a method of treating or preventing infection caused by an RNA-containing virus comprising administering to a patient in need of such treatment the pharmaceutical composition of the present invention.

Detailed Description of the Invention

As used in the present specification the following terms have the meanings indicated:

As used herein, the singular forms "a", "an", and "the" may include plural reference unless the context clearly dictates otherwise.

The term "alkyl," as used herein, refers to a group derived from a straight or branched chain saturated hydrocarbon containing 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms. Examples of alkyl groups include butyl, methyl, 2-methylbutyl, and the like.

The term "alkenyl," as used herein, refers to a straight or branched chain group of 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms containing at least one carbon-carbon double bond. Examples of alkenyl groups include allyl, propenyl, 3-methyl-2-butenyl, and the like.

The term "alkynyl," as used herein, refers to a straight or branched chain hydrocarbon of 2, 3, 4, 5, 6, 7, 8, 9 or 10 carbon atoms containing at least one carbon-carbon triple bond. Examples of alkynyl groups include ethynyl, 2-methyl-3-butynyl, 3-pentynyl, and the like.

The term "alkoxy," as used herein, refers to an alkyl group attached to the parent molecular moiety through an oxygen atom. Examples of alkoxy groups include tert-butoxy, methoxy, isopropoxy, and the like.

The term "alkoxyalkoxy" as used herein, means an alkoxy group, as defined herein, appended to the parent molecular moiety through another alkoxy group, as defined herein. Representative examples of alkoxyalkoxy include, but are not limited to, tert-butoxymethoxy, 2-ethoxyethoxy, 2-methoxyethoxy, and methoxymethoxy.

The term "alkoxyalkoxyalkyl" as used herein, means an alkoxyalkoxy group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkoxyalkoxyalkyl include, but are not limited to, tert-butoxymethoxymethyl, ethoxymethoxymethyl, (2-methoxyethoxy)methyl, and 2-(2-methoxyethoxy)ethyl.

The term "alkoxyalkyl," as used herein, refers to an alkyl group substituted by at least one alkoxy group.

The term "alkoxycarbonyl," as used herein, refers to an alkoxy group attached to the parent molecular moiety through a carbonyl group. Examples of alkoxycarbonyl groups include tert-butoxycarbonyl, ethoxycarbonyl, methoxycarbonyl, and the like.

The term "alkoxycarbonylalkyl," as used herein, refers to an alkoxycarbonyl group attached to the parent molecular moiety through an alkyl group.

The term "alkylcarbonyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a carbonyl group. Examples of alkylcarbonyl groups include acyl, butanoyl, 2,2-dimethylpropanoyl, and the like.

The term "alkylcarbonylalkyl" as used herein, means an alkylcarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein. Representative examples of alkylcarbonylalkyl include, but are not limited to, 2-oxopropyl, 3,3-dimethyl-2-oxopropyl, 3-oxobutyl, and 3-oxopentyl.

The term "alkylsulfanyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a sulfur atom. Examples of alkylsulfanyl groups include methylsulfanyl, (1-methylethyl)sulfanyl, (2-methylpropyl)sulfanyl, and the like.

The term "alkylsulfanylalkyl," as used herein, refers to an alkylsulfanyl group attached to the parent molecular moiety through an alkyl group.

The term "alkylsulfinyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a –S(O)- group.

The term "alkylsulfinylalkyl," as used herein, refers to an alkylsulfinyl group attached to the parent molecular moiety through an alkyl group.

The term "alkylsulfonyl," as used herein, refers to an alkyl group attached to the parent molecular moiety through a $-S(O)_2-$ group.

The term "alkylsulfonylalkyl," as used herein, refers to an alkylsulfonyl group attached to the parent molecular moiety through an alkyl group.

The term "aryl" as used herein, refers to a phenyl group, or a bicyclic or tricyclic hydrocarbon fused ring systems wherein one or more of the rings is a phenyl group. Bicyclic fused ring systems have a phenyl group fused to a monocyclic cycloalkenyl group, as defined herein, a monocyclic cycloalkyl group, as defined herein, or another phenyl group. Tricyclic fused ring systems are exemplified by a bicyclic fused ring system fused to a monocyclic cycloalkenyl group, as defined herein, a monocyclic cycloalkyl group, as defined herein, or another phenyl group. Examples of aryl groups include anthracenyl, azulenyl, fluorenyl, indanyl, indenyl, naphthyl, phenyl, tetrahydronaphthyl, and the like. The aryl groups of the present invention can be connected to the parent molecular moiety through any substitutable carbon atom of the group. The aryl groups of the present invention can be substituted with 0,

1, 2, 3, 4 or 5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, cycloalkenyl, heterocycle, a second aryl group and heteroaryl; wherein each of the alkyl, alkenyl and alkynyl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, cycloalkenyl, heterocycle, a second aryl group and heteroaryl; wherein R_a, R_b and R_e are defined herein, and wherein the second aryl group, the heteroaryl, the cycloalkyl, the cycloalkenyl and the heterocycle can be substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of –OH, -O(alkyl), alkyl, alkenyl, alkynyl, cyano, formyl, halo, haloalkoxy, haloalkyl, nitro, $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -C(O)OH, -C(O)O(alkyl), $-C(O)NH_2$, -C(O)N(H)(alkyl), $-C(O)N(alkyl)_2$ and oxo.

The term "arylalkenyl," as used herein, refers to an aryl group attached to the parent molecular moiety through an alkenyl group.

The term "arylalkoxy," as used herein, refers to an arylalkyl group attached to the parent molecular moiety through an oxygen atom.

The term "arylalkyl," as used herein, refers to an aryl group attached to the parent molecular moiety through an alkyl group.

The term "arylcarbonyl," as used herein, refers to an aryl group attached to the parent molecular moiety through a carbonyl group.

The term "arylcarbonylalkyl" as used herein, means an arylcarbonyl group, as defined herein, appended to the parent molecular moiety through an alkyl group, as defined herein.

The term "aryloxy," as used herein, refers to an aryl group attached to the parent molecular moiety through an oxygen atom.

The term "aryloxyalkyl," as used herein, refers to an aryloxy group attached to the parent molecular moiety through an alkyl atom.

The term "arylsulfanyl," as used herein, refers to an aryl group attached to the parent molecular moiety through a sulfur atom.

The term "arylsulfanylalkyl," as used herein, refers to an arylsulfanyl group attached to the parent molecular moiety through an alkyl group.

The term "arylsulfonyl," as used herein, refers to an aryl group attached to the parent molecular moiety through a sulfonyl group.

The term "arylsulfonylalkyl," as used herein, refers to an arylsulfonyl group attached to the parent molecular moiety through an alkyl group.

The term "carboxy," as used herein, refers to $-CO_2H$.

The term "carboxyalkyl," as used herein, refers to a carboxy group attached to the parent molecular moiety through an alkyl group.

The term "cyano," as used herein, refers to -CN.

The term "cyanoalkyl," as used herein, refers to a cyano group attached to the parent molecular moiety through an alkyl group.

The term "cycloalkenyl," as used herein, refers to a non-aromatic, partially unsaturated, monocyclic, bicyclic or tricyclic ring system, having three to fourteen carbon atoms and zero heteroatom. Examples of cycloalkenyl groups include cyclohexenyl, octahydronaphthalenyl, norbornylenyl, and the like. The cycloalkenyl groups of the present invention can be substituted with 0, 1, 2, 3, 4 or 5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$ cycloalkyl, a second cycloalkenyl, heterocycle, aryl, heteroaryl and ethylenedioxy; wherein each of the alkyl, alkenyl and alkynyl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, a second cycloalkenyl, heterocycle, aryl and heteroaryl; wherein R_a, R_b and R_e are defined herein, and wherein the cycloalkyl, the second cycloalkenyl, the heterocycle, the aryl and the heteroaryl can be substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of –OH, -O(alkyl), alkyl, alkenyl, alkynyl, cyano, formyl, halo, oxo, haloalkoxy, haloalkyl, nitro, oxo, $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -C(O)OH, -C(O)O(alkyl), $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$.

The term "cycloalkenylalkyl," as used herein, refers to a cycloalkenyl group attached to the parent molecular moiety through an alkyl group.

The term "cycloalkyl," as used herein, refers to a saturated monocyclic, bicyclic, or tricyclic hydrocarbon ring system having three to fourteen carbon atoms and zero heteroatom. Examples of cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, bicyclo[3.1.1]heptyl, 6,6-dimethylbcyclo[3.1.1]heptyl, adamantyl, and the like. The cycloalkyl groups of the present invention can be substituted with 0, 1, 2, 3,

4 or 5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, a second cycloalkyl, cycloalkenyl, heterocycle, aryl, heteroaryl and ethylenedioxy; wherein each of the alkyl, alkenyl and alkynyl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, a second cycloalkyl, cycloalkenyl, heterocycle, aryl and heteroaryl; wherein R_a, R_b and R_e are defined herein, and wherein the second cycloalkyl, the cycloalkenyl, the heterocycle, the aryl and the heteroaryl can be substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of –OH, -O(alkyl), alkyl, alkenyl, alkynyl, cyano, formyl, halo, haloalkoxy, haloalkyl, nitro, oxo, $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -C(O)OH, -C(O)O(alkyl), $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$.

The term "cycloalkylalkenyl," as used herein, refers to a cycloalkyl group attached to the parent molecular moiety through an alkenyl group.

The term "cycloalkylalkyl," as used herein, refers to a cycloalkyl group attached to the parent molecular moiety through an alkyl group.

The term "formyl," as used herein, refers to -CHO.

The term "formylalkyl," as used herein, refers to a formyl group attached to the parent molecular moiety through an alkyl group.

The terms "halo," and "halogen," as used herein, refer to F, Cl, Br, and I.

The term "haloalkoxy," as used herein, refers to a haloalkyl group attached to the parent molecular moiety through an oxygen atom.

The term "haloalkoxyalkyl," as used herein, refers to a haloalkoxy group attached to the parent molecular moiety through an alkyl group.

The term "haloalkyl," as used herein, refers to an alkyl group substituted by one, two, three, or four halogen atoms.

The term "heteroaryl," as used herein, refers to an aromatic five- or six-membered ring where at least one atom is selected from the group consisting of N, O, and S, and the remaining atoms are carbon. The term "heteroaryl" also includes bicyclic systems where a heteroaryl ring is fused to a phenyl group, a monocyclic cycloalkyl group, as defined herein, a heterocycle group, as defined herein, or an additional heteroaryl group. The term "heteroaryl" also includes tricyclic systems where a bicyclic system is fused to a phenyl

group, a monocyclic cycloalkyl group, as defined herein, a heterocycle group, as defined herein, or an additional heteroaryl group. The heteroaryl groups are connected to the parent molecular moiety through any substitutable carbon or nitrogen atom in the groups. Examples of heteroaryl groups include benzothienyl, benzoxazolyl, benzimidazolyl, benzoxadiazolyl, dibenzofuranyl, dihydrobenzothiazolyl, furanyl, imidazolyl, indazolyl, indolyl, isoindolyl, isoxazolyl, isoquinolinyl, isothiazolyl, oxadiazolyl, oxazolyl, thiazolyl, thienopyridinyl, thienyl, triazolyl, thiadiazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrazolyl, pyrrolyl, quinolinyl, tetrahydroquinolinyl, tetrahydropyranyl, triazinyl, and the like. The heteroaryl groups of the present invention can be substituted with 0, 1, 2, 3, 4 or 5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, cycloalkenyl, heterocycle, aryl and a second heteroaryl group; wherein each of the alkyl, alkenyl and alkynyl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, cycloalkenyl, heterocycle, aryl and a second heteroaryl group; wherein R_a, R_b and R_e are defined herein, and wherein the second heteroaryl group, the aryl, the cycloalkyl, the cycloalkenyl and the heterocycle can be independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of –OH, -O(alkyl), alkyl, alkenyl, alkynyl, cyano, formyl, halo, haloalkoxy, haloalkyl, nitro, $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -C(O)OH, -C(O)O(alkyl), $-C(O)NH_2$, -C(O)N(H)(alkyl), $-C(O)N(alkyl)_2$ and oxo. In addition, The nitrogen heteroatoms can be optionally quaternized or oxidized to the N-oxide. Also, the nitrogen containing rings can be optionally N-protected.

The term "heteroarylalkenyl," as used herein, refers to a heteroaryl group attached to the parent molecular moiety through an alkenyl group.

The term "heteroarylalkyl," as used herein, refers to a heteroaryl group attached to the parent molecular moiety through an alkyl group.

The term "heteroarylsulfonyl," as used herein, refers to a heteroaryl group attached to the parent molecular moiety through a sulfonyl group.

The term "heteroarylsulfonylalkyl," as used herein, refers to a heteroarylsulfonyl group attached to the parent molecular moiety through a alkyl group.

The term "heterocycle," as used herein, refers to cyclic, non-aromatic, saturated or

partially unsaturated, three, four, five-, six-, or seven-membered rings containing at least one atom selected from the group consisting of oxygen, nitrogen, and sulfur. The term "heterocycle" also includes bicyclic systems where a heterocycle ring is fused to a phenyl group, a monocyclic cycloalkenyl group, as defined herein, a monocyclic cycloalkyl group, as defined herein, or an additional monocyclic heterocycle group. The term "heterocycle" also includes tricyclic systems where a bicyclic system is fused to a phenyl group, a monocyclic cycloalkenyl group, as defined herein, a monocyclic cycloalkyl group, as defined herein, or an additional monocyclic heterocycle group. The heterocycle groups of the invention are connected to the parent molecular moiety through any substitutable carbon or nitrogen atom in the group. Examples of heterocycle groups include benzoxazinyl, dihydroindolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, isoindolinyl, morpholinyl, piperazinyl, pyrrolidinyl, tetrahydropyridinyl, piperidinyl, thiomorpholinyl, tetrahydropyranyl, and the like. The heterocycle groups of the present invention can be substituted with 0, 1, 2, 3, 4 or 5 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, cycloalkenyl, a second heterocycle, aryl, heteroaryl and ethylenedioxy; wherein each of the alkyl, alkenyl and alkynyl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of cyano, formyl, halo, nitro, oxo, $-OR_a$, $-OC(O)R_a$, $-OC(O)OR_a$, $-OC(O)NR_aR_b$, $-OSO_2R_a$, $-OSO_2NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-SO_2OR_a$, $-SO_2NR_aR_b$, $-NR_aR_b$, $-N(R_e)C(O)R_a$, $-N(R_e)C(O)OR_a$, $-N(R_e)C(O)NR_aR_b$, $-N(R_e)SO_2R_a$, $-N(R_e)SO_2NR_aR_b$, $-N(R_e)SO_2N(R_e)C(O)OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$, cycloalkyl, cycloalkenyl, a second heterocycle, aryl and heteroaryl; wherein R_a, R_b and R_e are defined herein, and wherein the cycloalkyl, cycloalkenyl, the second heterocycle, the aryl and the heteroaryl can beindependently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of –OH, -O(alkyl), alkyl, alkenyl, alkynyl, cyano, formyl, halo, haloalkoxy, haloalkyl, nitro, oxo, $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -C(O)OH, -C(O)O(alkyl), $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$. In addition, The nitrogen heteroatoms can be optionally quaternized or oxidized to the N-oxide. Also, the nitrogen containing heterocyclic rings can be optionally N-protected.

The term "heterocyclealkenyl," as used herein, refers to a heterocycle group attached to the parent molecular moiety through an alkenyl group.

The term "heterocyclealkyl," as used herein, refers to a heterocycle group attached to the parent molecular moiety through an alkyl group.

The term "heterocyclecarbonyl" as used herein, means a heterocycle, as defined

herein, appended to the parent molecular moiety through a carbonyl group, as defined herein. Representative examples of heterocyclecarbonyl include, but are not limited to, pyrrolidinylcarbonyl and piperazin-1-ylcarbonyl.

The term "hydroxy," as used herein, refers to -OH.

The term "hydroxyalkyl," as used herein, refers to an alkyl group substituted by at least one hydroxy group.

The term "nitro," as used herein, refers to $-NO_2$.

The term "nitroalkyl," as used herein, refers to an alkyl group substituted by at least one nitro group.

The term "oxo," as used herein, refers to =O.

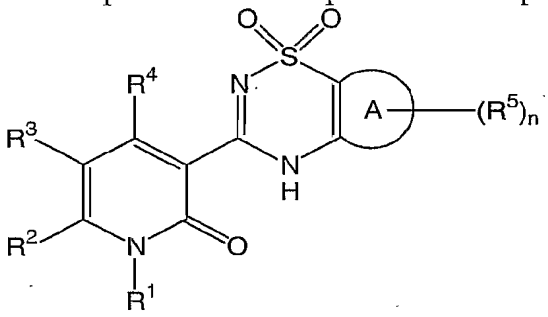
The term "sulfanyl," as used herein, refers to -S-.

The term "sulfinyl," as used herein, refers to -SO-.

The term "sulfonyl," as used herein, refers to $-SO_2-$.

It is understood that alkenyl, alkoxy, alkoxyalkoxy, alkoxyalkoxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonyalkyl, alkynyl, alkylsulfanyl, alkylsulfanylalkyl, alkylsulfinyl, alkylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylalkenyl, arylalkoxy, arylalkyl, aryloxyalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenylalkyl, cycloalkenylalkenyl, cycloalkylalkyl, formylalkyl, haloalkoxy, haloalkoxyalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterosulfonylalkyl, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl and nitroalkyl may optionally be substituted.

In a first embodiment the present invention provides a compound of formula (I)



(I)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

A is a monocyclic or bicyclic ring selected from the group consisting of aryl, cycloalkyl, cycloalkenyl, heteroaryl and heterocycle;

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl,

(cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, R_fR_gC=N- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, -$N(R_a)(R_b)$, $R_aR_bNC(O)$-, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$ and $R_aC(O)$-; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$;

alternatively, R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is independently substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bN$alkyl-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)$alkyl-, $R_aSO_2N(R_f)$alkyl-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)$alkyl-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)$alkyl-, R_kOalkyl-, $R_aR_bNSO_2$-, $R_aR_bNSO_2$alkyl-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle,

arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -S(O)R_a, -$S(O)_2R_a$, -OR_k, -N(R_a)(R_b), -C(O)R_a, -C(O)OR_a and -C(O)NR_aR_b; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -C(O)OR_a, -C(O)NR_aR_b and -NC(O)R_a;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kO$alkyl-, R_cR_dNalkyl-, R_cR_dNC(O)alkyl-, R_cSO_2-, $R_cSO_2$alkyl-, $R_cC(O)$-, $R_cC(O)$alkyl-, $R_cOC(O)$-, $R_cOC(O)$alkyl-, R_cR_dNalkylC(O)-, R_cR_dNC(O)-, R_cR_dNC(O)Oalkyl-, R_cR_dNC(O)N(R_e)alkyl-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -alkyl$SO_2NR_cR_d$, -alkylC(O)NR_cR_d, -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -CO(R_f), -SR_f, -SOR_f, -SO_2R_f, -C(O)NR_fR_h, -$SO_2NR_fR_h$, -C(O)OR_f, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -N(R_f)(R_h), -C(O)R_f, -C(O)OR_f, -C(O)NR_fR_h, -C(O)N(H)NR_fR_h, -N(R_e)C(O)OR_f, -N(R_e)$SO_2NR_fR_h$, -N(R_e)C(O)NR_fR_h, -alkylN(R_e)C(O)OR_f, -alkylN(R_e)$SO_2NR_fR_h$, and -alkylN(R_e)C(O)NR_fR_h;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and

heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -N(R_f)(R_h), -C(O)R_f, -C(O)OR_f and -C(O)NR_fR_h;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)$N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

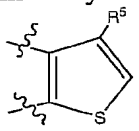
alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkyl$N(alkyl)_2$, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)$N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, R_aS(O)-, R_aSO_2-, R_aSalkyl-, R_a(O)Salkyl-, $R_aSO_2$alkyl-, R_aOC(O)-, R_aOC(O)alkyl-, R_aC(O)-, R_aC(O)alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

m is 0, 1, 2, 3, or 4; and

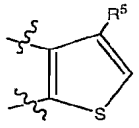
n is 0, 1, 2, 3, or 4;

with the proviso that when A is a monocyclic ring other than



and R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or -OR_k, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl;

and with the further proviso that when A is



and R^4 is hydroxy or R_eS-, and R^5 is hydrogen, unsubstituted alkyl, halo or -OR_k, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (I) wherein A is a monocyclic ring selected from the group consisting of aryl and heteroaryl.

For example, the present invention provides a compound of formula (I) wherein A is a bicyclic ring selected from the group consisting of heterocycle and heteroaryl.

For example, the present invention provides a compound of formula (I) wherein A is selected from the group consisting of naphthyl, indolizinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, benzthiazolyl, benzoxazolyl, benzoisothiazolyl, benzoisoxazolyl, benzoxazinyl, benzothiadiazolyl, quinolinyl, isoquinolinyl, quinazolinyl, quinoxalinyl and naphthyridinyl, cinnolinyl and pteridinyl.

For example, the present invention provides a compound of formula (I) wherin R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of thienyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl,

phenyl, pyridyl, pyridazinyl and pyrimidinyl.

For example, the present invention provides a compound of formula (I) wherein R^2 and R^3 together with the carbon atoms to which they are attached form a cycloalkyl ring.

For example, the present invention provides a compound of formula (I) wherein R^2 and R^3 together with the carbon atoms to which they are attached form a cyclopentyl or cyclohexyl ring.

For example, the present invention provides a compound of formula (I) wherein R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, $-N(R_a)(R_b)$, $R_aR_bNC(O)-$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$ and $R_aC(O)-$; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, $-(alkyl)(OR_k)$, $-(alkyl)(NR_aR_b)$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$.

For example, the present invention provides a compound of formula (I) wherein R^4 is hydroxy, halo, $-NH_2$,$-NH(alkyl)$, $-N(alkyl)_2$, $-N(H)NH_2$, $-N_3$, $-N(H)(hydroxyalkyl)$, or R_cS-.

For example, the present invention provides a compound of formula (I) wherein A is aryl and R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, thienyl, furanyl, pyrazolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, tetrazolyl, cyclopentyl and cyclohexyl.

For example, the present invention provides a compound of formula (I) wherein A is phenyl and R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, thienyl, furanyl, pyrazolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, tetrazolyl, cyclopentyl and cyclohexyl.

For example, the present invention provides a compound of formula (I) wherein A is phenyl and R^2 and R^3, together with the carbon atoms to which they are attached is pyridyl.

For example, the present invention provides a compound of formula (I) wherein A is phenyl and R^2 and R^3, together with the carbon atoms to which they are attached is thienyl.

For example, the present invention provides a compound of formula (I) wherein A is heteroaryl and R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, pyrazolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, tetrazolyl, cyclopentyl and cyclohexyl.

For example, the present invention provides a compound of formula (I) wherein A is thienyl and R^2 and R^3, together with the carbon atoms to which they are attached form a five-

or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, pyrazolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, tetrazolyl, cyclopentyl and cyclohexyl.

For example, the present invention provides a compound of formula (I) wherein A is thienyl, and R^2 and R^3 together with the carbon atoms to which they are attached form a phenyl ring.

For example, the present invention provides a compound of formula (I) wherein A is thienyl, and R^2 and R^3, together with the carbon atoms to which they are attached is pyridyl.

For example, the present invention provides a compound of formula (I) wherein A is pyridyl, and R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, thienyl, furanyl, pyrrolyl, pyrazolyl, oxazolyl, thiazolyl, imidazolyl, isoxazolyl, isothiazolyl, triazolyl, thiadiazolyl, tetrazolyl, cyclopentyl and cyclohexyl.

For example, the present invention provides a compound of formula (I) wherein A is pyridyl, and R^2 and R^3 together with the carbon atoms to which they are attached form a pyridyl ring.

For example, the present invention provides a compound of formula (I) wherein A is phenyl, thienyl, pyridyl, imidazolyl, benzoxazolyl, benzoxazinyl, or benzimidazolyl, and R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, $-N(R_a)(R_b)$, $R_aR_bNC(O)-$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$ and $R_aC(O)-$; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, $-(alkyl)(OR_k)$, $-(alkyl)(NR_aR_b)$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$.

For example, the present invention provides a compound of formula (I) wherein R^2 and R^3 together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of thienyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxadiazolyl, triazolyl, thiadiazolyl, tetrazolyl, phenyl, pyridyl, pyridazinyl and pyrimidinyl, and R^4 is hydroxy. In an even more preferred embodiment, the present invention provides a compound of formula (I) wherein A is pyridyl, phenyl, thienyl, imidazolyl, benzoxazolyl, benzimidazolyl or benzoxazinyl, R^2 and R^3 together with the carbon atoms to which they are attached form a five- or six- membered ring selected from phenyl, thienyl, pyrazolyl, pyridyl, pyrimidinyl or pyridazinyl, and R^4 is hydroxy.

For example, the present invention provides a compound of formula (I) wherein A is pyridyl; R^2 and R^3, together with the carbon atoms to which they are attached, form a pyridyl

ring; and R^4 is hydroxyl.

For example, the present invention provides a compound of formula (I) wherein A is pyridyl, phenyl, thienyl, imidazolyl, benzoxazolyl, benzimidazolyl or benzoxazinyl, R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, $-N(R_a)(R_b)$, $R_aR_bNC(O)-$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$ and $R_aC(O)-$; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, $-(alkyl)(OR_k)$, $-(alkyl)(NR_aR_b)$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$; and R^4 is hydroxy.

For example, the present invention provides a compound of formula (I) wherein A is pyridyl, phenyl, thienyl, imidazolyl, benzimidazolyl, benzoxazolyl or benzoxazinyl, R^2 and R^3 together with the carbon atoms to which they are attached form five- or six-membered ring selected from the group consisting of phenyl, pyridyl, thienyl, pyrimidinyl, pyrazolyl, pyridazinyl, cyclohexyl or cyclopentyl, R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, $R_aR_bNalkyl-$, $R_aR_bNC(O)alkyl-$, $R_fR_gC=N-$ and R_kO-.

Examplary compounds of the first embodiment of the present invention of formula (I) include, but not limited to, the following:

1-[2-(1-cyclohexen-1-yl)ethyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one;

ethyl [3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]acetate;

1-(3-anilinopropyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one;

3-[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]propanal;

1-[3-(dimethylamino)propyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one;

1-{3-[[2-(dimethylamino)ethyl](methyl)amino]propyl}-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one;

1-(2-aminoethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one;

1-[3-(diethylamino)propyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-

hydroxy-1,8-naphthyridin-2(1H)-one;

1-(benzyloxy)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one;

1-(benzyloxy)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-isobutoxy-1,8-naphthyridin-2(1H)-one;

1-benzyl-4-chloro-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

1-butyl-4-chloro-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

4-amino-1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-(methylamino)-1,8-naphthyridin-2(1H)-one;

1-butyl-4-(dimethylamino)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydrazino-1,8-naphthyridin-2(1H)-one;

4-azido-1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-[(2-hydroxyethyl)amino]-1,8-naphthyridin-2(1H)-one;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-*N*'-(2-phenylethyl)sulfamide;

benzyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

benzyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-propyldiazathiane-1-carboxylate 2,2-dioxide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-*N*'-propylsulfamide;

methyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

allyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

2-propynyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

2-cyanoethyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

2-(trimethylsilyl)ethyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

benzyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

methyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

benzyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-methyldiazathiane-1-carboxylate 2,2-dioxide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-*N*'-methylsulfamide;

2-aminoethyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

N-cyclopentyl-*N*'-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

N-cyclobutyl-*N*'-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-*N*'-(4-piperidinyl)sulfamide;

N-(2-hydroxyethyl)-*N*'-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

3-[({[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]amino}sulfonyl)amino]propanamide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-azetidinesulfonamide;

3-hydroxy-*N*-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-azetidinesulfonamide;

3-amino-*N*-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-pyrrolidinesulfonamide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-piperidinesulfonamide;

N-benzyl-*N*'-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

ethyl 3-[({[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]amino}sulfonyl)amino]benzoate;

3-[({[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]amino}sulfonyl)amino]benzoic acid;

3-[({[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]amino}sulfonyl)amino]benzamide;

N-(2-aminoethyl)-*N*'-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

ethyl 1-({[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]amino}sulfonyl)-3-piperidinecarboxylate;

methyl (2*S*)-1-({[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]amino}sulfonyl)-2-pyrrolidinecarboxylate;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-pyrrolidinesulfonamide;

3-hydroxy-*N*-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]-1-piperidinesulfonamide;

N-(2-furylmethyl)-3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro[1,8]naphthyridin-3-yl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxamide 2,2-dioxide;

4-amino-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-Dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-(isobutylamino)thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-{[(3*S*)-3-methylcyclopentyl]amino}thieno[3,2-*b*]pyridin-5(4*H*)-one;

4-{[1-cyclopropylethyl]amino}-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(butylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-[(2-ethylbutyl)amino]-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-(pentylamino)thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(3-methylbutyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

4-[(3,3-dimethylbutyl)amino]-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(3-

methylbenzyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(2-methylbenzyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(4-methylbenzyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(3-methylbut-2-enyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-(propylamino)thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(pyridin-4-ylmethyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(pyridin-3-ylmethyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(pyridin-2-ylmethyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(3-methoxybenzyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-[(3-furylmethyl)amino]-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

3-({[6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-5-oxothieno[3,2-*b*]pyridin-4(5*H*)-yl]amino}methyl)benzonitrile;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(thien-3-ylmethyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(cyclobutylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(benzylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-[(cyclohexylmethyl)amino]-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-[(1,3-thiazol-5-ylmethyl)amino]thieno[3,2-*b*]pyridin-5(4*H*)-one;

4-[(3-bromobenzyl)amino]-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(cyclohexylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(cyclopentylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(cycloheptylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-{[(1*R*,3*S*)-3-methylcyclohexyl]amino}thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-{[(1*R*,3*R*)-3-methylcyclohexyl]amino}thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-[(1-ethylpropyl)amino]-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-{[1-phenylethyl]amino}thieno[3,2-*b*]pyridin-5(4*H*)-one;

6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxy-4-{[(1*R*)-1-methylbutyl]amino}thieno[3,2-*b*]pyridin-5(4*H*)-one;

4-(cyclobutylamino)-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

4-[(cyclopropylmethyl)amino]-6-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-*b*]pyridin-5(4*H*)-one;

2-({3-[4-(cyclohexylamino)-7-hydroxy-5-oxo-4,5-dihydrothieno[3,2-*b*]pyridin-6-yl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

N-({3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl]-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-7-yl}methyl)urea;

1-benzyl-4-hydroxy-3-{7-[(methoxymethoxy)methyl]-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-3-yl}quinolin-2(1*H*)-one;

1-Benzyl-4-hydroxy-3-[7-(hydroxymethyl)-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-3-yl]quinolin-2(1*H*)-one;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4*H*-thieno[2,3-*e*][1,2,4]thiadiazine-7-carboxylic acid 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4*H*-thieno[2,3-*e*][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-*N*-(2-hydroxyethyl)-4*H*-thieno[2,3-*e*][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-*N*-[(1*S*)-2-hydroxy-1-(aminocarbonyl)ethyl]-4*H*-thieno[2,3-*e*][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

N-(2-amino-2-oxoethyl)-3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4*H*-thieno[2,3-*e*][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[(1S)-2-hydroxy-1-methylethyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N,N-bis(2-hydroxyethyl)-

4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[2-hydroxy-1-(hydroxymethyl)ethyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

1-benzyl-4-hydroxy-3-(7-{[(3R)-3-hydroxypyrrolidin-1-yl]carbonyl}-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-3-yl)quinolin-2(1H)-one;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-(3-hydroxypropyl)-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[(2S)-2,3-dihydroxypropyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[(1S)-1-(hydroxymethyl)propyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[(1S)-1-(hydroxymethyl)-2-methylpropyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[2-hydroxybutyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-N-[2-hydroxy-2-(4-hydroxyphenyl)ethyl]-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

1-benzyl-3-[1,1-dioxido-7-(piperazin-1-ylcarbonyl)-4H-thieno[2,3-e][1,2,4]thiadiazin-3-yl]-4-hydroxyquinolin-2(1H)-one;

N-[5-(aminocarbonyl)pyridin-2-yl]-3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-4H-thieno[2,3-e][1,2,4]thiadiazine-7-carboxamide 1,1-dioxide;

[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-7-yl]methyl carbamate;

[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-7-yl]methyl aminocarbonylcarbamate;

3-[7-(azidomethyl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-3-yl]-1-benzyl-4-hydroxyquinolin-2(1H)-one;

3-[7-(aminomethyl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-3-yl]-1-benzyl-4-hydroxyquinolin-2(1H)-one;

N-{[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl]methyl}methanesulfonamide;

N-{[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl]methyl}nicotinamide;

N-{[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl]methyl}morpholine-4-carboxamide;

N-{[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl]methyl}-2-hydroxyacetamide;

1-[(cyclopropylmethyl)amino]-4-hydroxy-3-{7-[(methoxymethoxy)methyl]-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-3-yl}quinolin-2(1H)-one;

1-[(cyclopropylmethyl)amino]-4-hydroxy-3-[7-(hydroxymethyl)-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-3-yl]quinolin-2(1H)-one;

N-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl)methyl]methanesulfonamide;

N-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl)methyl]ethanesulfonamide;

N-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-thieno[2,3-e][1,2,4]thiadiazin-7-yl)methyl]propane-1-sulfonamide;

N-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-7-yl)methyl]propane-2-sulfonamide;

N-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-7-yl)methyl]benzenesulfonamide;

N-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-7-yl)methyl]-1-phenylmethanesulfonamide;

1-butyl-4-hydroxy-3-{7-[(methoxymethoxy)methyl]-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-3-yl}-1,8-naphthyridin-2(1*H*)-one;

1-butyl-4-hydroxy-3-[7-(hydroxymethyl)-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-3-yl]-1,8-naphthyridin-2(1*H*)-one;

methyl 3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl)-4*H*-thieno[2,3-*e*][1,2,4]thiadiazine-7-carboxylate 1,1-dioxide;

4-hydroxy-3-{7-[(methoxymethoxy)methyl]-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-3-yl}-1-(3-methylbutyl)-1,8-naphthyridin-2(1*H*)-one;

4-hydroxy-3-[7-(hydroxymethyl)-1,1-dioxido-4*H*-thieno[2,3-*e*][1,2,4]thiadiazin-3-yl]-1-(3-methylbutyl)-1,8-naphthyridin-2(1*H*)-one;

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2(1H)-pyridinone;

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-5,6-dimethyl-2(1H)-pyridinone;

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-6-methyl-5-phenyl-2(1H)-pyridinone;

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-5,6-dimethyl-1-(3-methylbutyl)-2(1H)-pyridinone;

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(2-ethylbutyl)-4-hydroxy-5,6-dimethyl-2(1H)-pyridinone;

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-6-phenyl-2(1H)-

pyridinone;

1,5-dibenzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-6-methyl-2(1H)-pyridinone;

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(2-ethylbutyl)-4-hydroxy-6-methyl-5-phenyl-2(1H)-pyridinone;

1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-2(1H)-pyridinone;

N-{3-[4-hydroxy-1-(3-methylbutyl)-2-oxo-1,2-dihydropyridin-3-yl]-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl}methanesulfonamide;

N-[3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydropyridin-3-yl)-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl]methanesulfonamide;

N-[3-(4-hydroxy-2-oxo-1,2-dihydro-3-pyridinyl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]methanesulfonamide;

N-[3-(4-hydroxy-1-isopentyl-5,6-dimethyl-2-oxo-1,2-dihydro-3-pyridinyl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]methanesulfonamide;

benzyl 3-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro-3-pyridinyl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]diazathiane-1-carboxylate 2,2-dioxide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-1,2-dihydro-3-pyridinyl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]sulfamide;

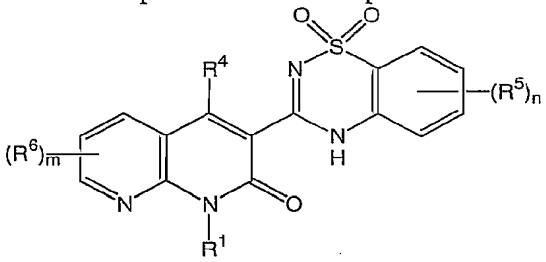
N-{3-[1-(cyclobutylmethyl)-4-hydroxy-2-oxo-1,2-dihydro-3-pyridinyl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}methanesulfonamide;

N-{3-[5-bromo-1-(cyclobutylmethyl)-4-hydroxy-2-oxo-1,2-dihydro-3-pyridinyl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}methanesulfonamide;

N-[3-(4-hydroxy-1-isopentyl-2-oxo-5-vinyl-1,2-dihydro-3-pyridinyl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]methanesulfonamide; and

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-propoxyquinolin-2(1*H*)-one; or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof.

In a second embodiment the present invention provides a compound of formula (II)



(II)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl,

alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, R_fR_gC=N- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is independently substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, R_aR_bNalkyl-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)$alkyl-, $R_aSO_2N(R_f)$alkyl-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)$alkyl-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)$alkyl-, R_kOalkyl-, $R_aR_bNSO_2$-, $R_aR_bNSO_2$alkyl-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl,

heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$, -$alkylC(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -$alkylN(R_e)C(O)OR_f$, -$alkylN(R_e)SO_2NR_fR_h$, and -$alkylN(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and

heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), $-SO_2$alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkyl$N(alkyl)_2$, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, $R_aS(O)$-, R_aSO_2-, R_aSalkyl-, R_a(O)Salkyl-, $R_aSO_2$alkyl-, $R_aOC(O)$-, $R_aOC(O)$alkyl-, $R_aC(O)$-, $R_aC(O)$alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

m is 0, 1, 2, 3, or 4; and

n is 0, 1, 2, 3, or 4;

with the proviso that when R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl,

heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (II) wherein R^4 is hydroxy.

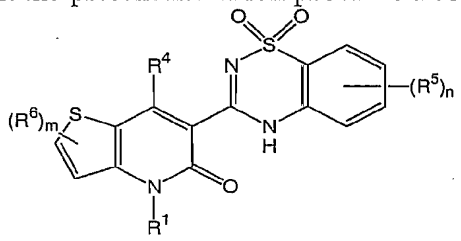
For example, the present invention provides a compound of formula (II) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_fR_gC=N$- and R_kO-.

For example, the present invention provides a compound of formula (II) wherein R^4 is hydroxy and R^1 is selected from the group consisting of, C3 alkyl, C4 alkyl, C5 alkyl, C3 alkenyl, C4 alkenyl, C5 alkenyl, C3 alkynyl, C4 alkynyl, C5 alkynyl, furyl(C1-C2 alkyl)-, thienyl(C1-C2 alkyl)-, phenyl(C1-C2 alkyl)-, pyridinyl(C1-C2 alkyl)-, thiazolyl(C1-C2 alkyl)-, isoxazolyl(C1-C2alkyl)-, naphthyl(C1-C2 alkyl), benzothienyl(C1-C2 alkyl)-, indolyl(C1-C2 alkyl)-, (C3-C7 cycloalkyl)(C1-C2 alkyl)-, (C5-C6 cycloalkenyl)(C1-C2 alkyl)-, C3-C7 cycloalkyl, (phenylalkyl)O-, (C1-C6 alkyl)O-, ((C3-C6 cycloalkyl)alkyl)O-, phenylCH=N-, NH_2, (C1-C7 alkyl)N(H)-, (C1-C7 alkenyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)alkyl)N(H)-, (phenylalkyl)N(H)-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (tetrahydropyran)N(H)-, (benzyl)N(H)-, (tetrahydronaphthalenyl)N(H)-, wherein each R^1 is substituted with 0, 1, 2, or 3 substituents selected from the group consisting of alkyl, hydroxy, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, phenyl, piperazinyl, morphilinyl, carboxy, -C(O)O(alkyl), $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -Oalkyl, -O-phenyl.

For example, the present invention provides a compound of formula (II) wherein R^4 is hydroxy and R^1 is selected from the group consisting of ((1-isopropyl)butyl)N(H)-, ((2-chloro-1,3-thiazol-5-yl)methyl)N(H)-, ((2-methyl-1,3-thiazol-4-yl)methyl)N(H)-, ((3-methylthien-2-yl)methyl)N(H)-, ((3-trifluoromethyl)cyclohexyl)N(H)-, ((5-chlorothien-2-yl)methyl)N(H)-, ((pyridin-3-yl)methyl)N(H)-, (1,2,3,4-tetrahydronaphthalen-2-yl)N(H)-, (1,3-thiazol-2-ylmethyl)N(H)-, (1,3-thiazol-5-ylmethyl)N(H)-, (1-cyclohezen-1-yl)ethyl, (1-cyclopropylethyl)N(H)-, (1-ethylbutyl)N(H)-, (1-ethylpropyl)N(H)-, (1-methylbutyl)N(H)-, (1-phenylethyl)N(H)-, (1-propylbutyl)N(H)-, (1-thien-3-ylethyl)N(H)-, (2-(1H-indol-3-yl)ethyl, (2-(dimethylamino)ethyl)(methyl)aminopropyl, (2-bromobenzyl)N(H)-, (2-chloro-1,3-thiazol-5-yl)methyl, (2-chloro-4-pyridinyl)methyl, (2-ethyl-3-methylbutyl)N(H)-, (2-ethylbutyl)N(H)-, (2-furylmethyl)N(H)-, (2-methyl-1,2-thiazol-4-yl)methyl, (2-methyl-1,3-thiazol-4-yl)methyl, (2-methyl-1,3-thiazol-5-yl)methyl, ((2-methylphenyl)methyl)N(H)-, (3,3-dimethylbutyl)N(H)-, (3,5-dimethyl-4-isoxazolyl)methyl, (3,5-

dimethylcyclohexyl)N(H)-, (3-bromobenzyl)N(H)-, (3-cyanobenzyl)N(H)-, (3-ethylcyclopentyl)N(H)-, (3-furylmethyl)N(H)-, ((3-methoxyphenyl)methyl)N(H)-, (3-methylbenzyl)N(H)-, (3-methylbut-2-enyl)N(H)-, (3-methylbutyl)N(H)-, (3-methylcyclohexyl)N(H)-, (3-methylcyclopentyl)N(H)-, (3-trifluoromethyl)benzyl, ((4-bromophenyl)methyl)N(H)-, (4-isopropylcyclohexyl)N(H)-, ((4-methoxyphenyl)methyl)N(H)-, ((4-methylphenyl)methyl)N(H)-, (5-bromo-2-thienyl)methyl, (5-bromo-3-pyridinyl)methyl, (5-carboxy-2-furyl)methyl, (5-chloro-2-thienyl)methyl, (5-ethoxycarbonyl-2-furyl)methyl, (5-methyl-2-thienyl)methyl, (5-methyl-3-isoxazolyl)methyl, (5-methyl-3-pyridinyl)methyl, (5-nitro-2-furyl)methyl, (5-phenyl-2-thienyl)methyl, (5-tert-butyl-2-thienyl)methyl, (6,6-dimethylbicyclo[3.1.1]hept-2-yl)methyl, (6-ethoxy-2-pyridinyl)methyl, (6-methyl-2-pyridinyl)methyl, (cyclopropylmethyl)N(H)-, (pyridin-2-ylmethyl)N(H)-, (pyridin-3-ylmethyl)N(H)-, (pyridin-4-ylmethyl)N(H)-, (tetrahydro-2H-pyran-4-yl)N(H)-, (thien-2-ylmethyl)N(H)-, (thien-3-ylmethyl)N(H)-, 1,1'-biphenyl-4-ylmethyl, 1,3-thiazol-4-ylmethyl, 1-adamantylmethyl, 1-benzothien-2-ylmethyl, 1-ethylpropyl, 1-naphthylmethyl, 1-neopentyl, 1-phenylethyl, 2-(1,3-dioxolan-2-yl)ethyl, 2-(3-thienyl)ethyl, 2,3-dihydroxypropyl, 2-aminoethyl, 2-cyanobenzyl, 2-cyclohexylethyl, (2-methylphenyl)methyl, 2-methylbutyl, 2-naphthylmethyl, 2-phenylethyl, 2-phenylpropyl, 2-pyridinylmethyl, 3-(4-methyl-1-piperazinyl)propyl, 3-(4-morpholinyl)propyl, 3-(diethylamino)propyl, 3-(dimethylamino)propyl, 3-anilinopropyl, 3-bromobenzyl, 3-butenyl, 3-chlorobenzyl, 3-cyanobenzyl, 3-ethylbutyl, 3-fluorobenzyl, 3-hydroxybutyl, 3-hydroxypropyl, 3-iodobenzyl, 3-methoxybenzyl, 3-methoxycarbonylbenzyl, 3-methyl-2-butenyl, 3-methylbenzyl, 3-methylbutyl, 3-nitrobenzyl, 3-phenoxybenzyl, 3-pyridinylmethyl, 3-thienylmethyl, 4-bromobenzyl, 4-cyanobenzyl, 4-methoxybenzyl, 4-methyl-3-pentenyl, 4-methylbenzyl, 4-methylpentyl, 4-pyridinylmethyl, 4-tert-butylbenzyl, $-NH_2$, phenylmethyl, (phenylmethyl)N(H)-, benzyloxy, (butyl)N(H)-, (cyclobutyl)N(H)-, cyclobutylmethyl, cycloheptyl, (cycloheptyl)N(H)-, cyclohexyl, (cyclohexyl)N(H)-, cyclohexylmethyl, cyclopentyl, (cyclopentyl)N(H)-, cyclopropylmethyl, cyclopropylethyl, hydrogen, isobutoxy, (isobutyl)N(H)-, (isopropyl)N(H)-, n-butyl, pentyl, (pentyl)N(H)-, (phenylmethylene)N(H)-, prop-2-enyl, propan-3-al, propoxy and (propyl)N(H)-.

In a third embodiment the present invention provides a compound of formula (III):



(III)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bNalkyl$-, $R_aR_bNC(O)alkyl$-, $R_aR_bNC(O)Oalkyl$-, $R_aR_bNC(O)NR_calkyl$-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, -NH_2, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl,

cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$, -$alkylC(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -$alkylN(R_e)C(O)OR_f$, -$alkylN(R_e)SO_2NR_fR_h$, and -$alkylN(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group

consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylN(alkyl)$_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkylN(alkyl)$_2$, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, R_aS(O)-, R_aSO_2-, R_aSalkyl-, R_a(O)Salkyl-, $R_aSO_2$alkyl-, R_aOC(O)-, R_aOC(O)alkyl-, R_aC(O)-, R_aC(O)alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

m is 0, 1, or 2; and

n is 0, 1, 2, 3, or 4;

with the proviso that when R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or -OR_k, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR_a, -S(O)R_a, -$S(O)_2R_a$, -OR_k, -N(R_a)(R_b), -C(O)R_a,

-C(O)OR_a and -C(O)NR_aR_b, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

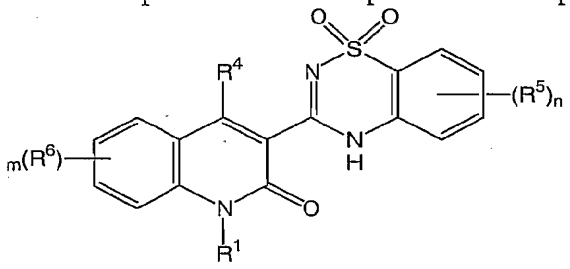
For example, the present invention provides a compound of formula (III) wherein R^4 is hydroxy.

For example, the present invention provides a compound of formula (III) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, R_aR_bNalkyl-, R_aR_bNC(O)alkyl-, R_fR_gC=N- and R_kO-.

For example, the present invention provides a compound of formula (III) wherein R^4 is hydroxy and R^1 is selected from the group consisting of ((1-isopropyl)butyl)N(H)-, ((2-chloro-1,3-thiazol-5-yl)methyl)N(H)-, ((2-methyl-1,3-thiazol-4-yl)methyl)N(H)-, ((3-methylthien-2-yl)methyl)N(H)-, ((3-trifluoromethyl)cyclohexyl)N(H)-, ((5-chlorothien-2-yl)methyl)N(H)-, ((pyridin-3-yl)methyl)N(H)-, (1,2,3,4-tetrahydronaphthalen-2-yl)N(H)-, (1,3-thiazol-2-ylmethyl)N(H)-, (1,3-thiazol-5-ylmethyl)N(H)-, (1-cyclohezen-1-yl)ethyl, (1-cyclopropylethyl)N(H)-, (1-ethylbutyl)N(H)-, (1-ethylpropyl)N(H)-, (1-methylbutyl)N(H)-, (1-phenylethyl)N(H)-, (1-propylbutyl)N(H)-, (1-thien-3-ylethyl)N(H)-, (2-(1H-indol-3-yl)ethyl, (2-(dimethylamino)ethyl)(methyl)aminopropyl, ((2-bromophenyl)methyl)N(H)-, (2-chloro-1,3-thiazol-5-yl)methyl, (2-chloro-4-pyridinyl)methyl, (2-ethyl-3-methylbutyl)N(H)-, (2-ethylbutyl)N(H)-, (2-furylmethyl)N(H)-, (2-methyl-1,2-thiazol-4-yl)methyl, (2-methyl-1,3-thiazol-4-yl)methyl, (2-methyl-1,3-thiazol-5-yl)methyl, (2_methylbenzyl)N(H)-, (3,3-dimethylbutyl)N(H)-, (3,5-dimethyl-4-isoxazolyl)methyl, (3,5-dimethylcyclohexyl)N(H)-, (3-bromobenzyl)N(H)-, (3-cyanobenzyl)N(H)-, (3-ethylcyclopentyl)N(H)-, (3-furylmethyl)N(H)-, (3-methoxybenzyl)N(H)-, (3-methylbenzyl)N(H)-, (3-methylbut-2-enyl)N(H)-, (3-methylbutyl)N(H)-, (3-methylcyclohexyl)N(H)-, (3-methylcyclopentyl)N(H)-, (3-trifluoromethyl)benzyl, ((4-bromophenyl)methyl)N(H)-, (4-isopropylcyclohexyl)N(H)-, ((4-methoxyphenyl)methyl)N(H)-, ((4-methylphenyl)methyl)N(H)-, (5-bromo-2-thienyl)methyl, (5-bromo-3-pyridinyl)methyl, (5-carboxy-2-furyl)methyl, (5-chloro-2-thienyl)methyl, (5-ethoxycarbonyl-2-furyl)methyl, (5-methyl-2-thienyl)methyl, (5-methyl-3-isoxazolyl)methyl, (5-methyl-3-pyridinyl)methyl, (5-nitro-2-furyl)methyl, (5-phenyl-2-thienyl)methyl, (5-tert-butyl-2-thienyl)methyl, (6,6-dimethylbicyclo[3.1.1]hept-2-yl)methyl, (6-ethoxy-2-pyridinyl)methyl, (6-methyl-2-pyridinyl)methyl, (cyclopropylmethyl)N(H)-, (pyridin-2-ylmethyl)N(H)-, (pyridin-3-ylmethyl)N(H)-, (pyridin-4-ylmethyl)N(H)-,

(tetrahydro-2H-pyran-4-yl)N(H)-, (thien-2-ylmethyl)N(H)-, (thien-3-ylmethyl)N(H)-, 1,1'-biphenyl-4-ylmethyl, 1,3-thiazol-4-ylmethyl, 1-adamantylmethyl, 1-benzothien-2-ylmethyl, 1-ethylpropyl, 1-naphthylmethyl, 1-neopentyl, 1-phenylethyl, 2-(1,3-dioxolan-2-yl)ethyl, 2-(3-thienyl)ethyl, 2,3-dihydroxypropyl, 2-aminoethyl, (2-cyanophenyl)methyl, 2-cyclohexylethyl, (2-methylphenyl)methyl, 2-methylbutyl, 2-naphthylmethyl, 2-phenylethyl, 2-phenylpropyl, 2-pyridinylmethyl, 3-(4-methyl-1-piperazinyl)propyl, 3-(4-morpholinyl)propyl, 3-(diethylamino)propyl, 3-(dimethylamino)propyl, 3-anilinopropyl, (3-bromophenyl)methyl, 3-butenyl, (3-chlorophenyl)methyl, (3-cyanophenyl)methyl, 3-ethylbutyl, (3-fluorophenyl)methyl, 3-hydroxybutyl, 3-hydroxypropyl, (3-iodophenyl)methyl, (3-methoxyphenyl)methyl, (3-methoxycarbonylphenyl)methyl, 3-methyl-2-butenyl, (3-methylphenyl)methyl, 3-methylbutyl, (3-nitrophenyl)methyl, 3-phenoxybenzyl, 3-pyridinylmethyl, 3-thienylmethyl, (4-bromophenyl)methyl, (4-cyanophenyl)methyl, (4-methoxyphenyl)methyl, 4-methyl-3-pentenyl, (4-methylphenyl)methyl, 4-methylpentyl, 4-pyridinylmethyl, (4-tert-butylphenyl)methyl, $-NH_2$, phenylmethyl, (phenylmethyl)N(H)-, (phenylethyl)N(H)-, benzyloxy, (butyl)N(H)-, (cyclobutyl)N(H)-, cyclobutylmethyl, cycloheptyl, (cycloheptyl)N(H)-, cyclohexyl, (cyclohexyl)N(H)-, cyclohexylmethyl, cyclopentyl, (cyclopentyl)N(H)-, cyclopropylethyl, cyclopropylmethyl, isobutoxy, (isobutyl)N(H)-, (isopropyl)N(H)-, n-butyl, pentyl, (pentyl)N(H)-, (phenylmethylene)N(H)-, prop-2-enyl, propan-3-al, propoxy and (propyl)N(H)-.

In a fourth embodiment the present invention provides a compound of formula (IV)



(IV)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl,

alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, -NH_2, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -alkyl$SO_2NR_cR_d$, -alkylC(O)NR_cR_d, -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -CO(R_f), -SR_f, -SOR_f, -SO_2R_f, -C(O)NR_fR_h, -$SO_2NR_fR_h$, -C(O)OR_f, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -N(R_f)(R_h), -C(O)R_f, -C(O)OR_f, -C(O)NR_fR_h, -C(O)N(H)NR_fR_h, -N(R_e)C(O)OR_f, -N(R_e)$SO_2NR_fR_h$, -N(R_e)C(O)NR_fR_h, -alkylN(R_e)C(O)OR_f, -alkylN(R_e)$SO_2NR_fR_h$, and -alkylN(R_e)C(O)NR_fR_h;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -N(R_f)(R_h), -C(O)R_f, -C(O)OR_f and -C(O)NR_fR_h;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, -OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylN(alkyl)$_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkyl$N(alkyl)_2$, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bN$alkyl-, $R_aO$alkyl-, $R_aR_bNC(O)$-, $R_aR_bNC(O)$alkyl, R_aS-, $R_aS(O)$-, R_aSO_2-, R_aSalkyl-, $R_a(O)$Salkyl-, $R_aSO_2$alkyl-, $R_aOC(O)$-, $R_aOC(O)$alkyl-, $R_aC(O)$-, $R_aC(O)$alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

m is 0, 1, 2, 3, or 4; and

n is 0, 1, 2, 3, or 4;

with the proviso that when R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (IV) wherein R^4 is hydroxy.

For example, the present invention provides a compound of formula (IV) wherein R^4 is hydroxy and R^1 is selected from the group consisting of R_aR_bN-, R_fR_gC=N- and R_kO-.

For example, the present invention provides a compound of formula (IV) wherein R^4 is hydroxy and R^1 is selected from the group consisting of alkylO-, (cycloalkyl)O-,

(arylalkyl)O-, arylCH=N-, -NH_2, alkylN(H)-, alkenylN(H)-, cycloalkylN(H)-, (cycloalkylalkyl)N(H)-, (heteroarylalkyl)N(H)-, (arylalkyl)N(H)- and (heterocycle)N(H)-.

For example, the present invention provides a compound of formula (IV) wherein R^4 is hydroxy and R^1 is selected from the group consisting of (C3-C7 alkyl)O-, (C3-C6 cycloalkyl)O-, (phenylalkyl)O-, phenylCH=N-, (C3-C7 alkyl)N(H)-, (C3-C7 alkenyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)C1-C2 alkyl)N(H)-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (tetranaphthalenyl)N(H)-, (tetrahydropyranyl)N(H)- and (phenylalkyl)N(H)-, wherein the phenyl, thienyl, thiazolyl, furyl and pyridinyl of (phenylalkyl)O-, phenylCH=N-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, and (phenylalkyl)N(H)- are each independently substituted with 0, 1 or 2 susbstituents selected from the group consisting of nitro, cyano, hydroxyl, alkoxy, -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, alkyl, halo, haloalkyl, carboxy, acetyl, and alkyoxycarbonyl.

For example, the present invention provides a compound of formula (IV) wherein R^4 is hydroxy and R^1 is selected from the group consisting of (phenylmethyl)N(H)-, (1-phenylethyl)N(H)-, (cycloproylmethyl)N(H)-, (cyclohexylmethyl)N(H)-, (1-cyclopropylethyl)N(H)-, phenylCH=N-, propylO-, (1-propylbutyl)N(H)-, (isobutyl)N(H)-, (isopropyl)N(H)-, (1-ethylpropyl)N(H)-, (1-ethylbutyl)N(H)-, (2-ethylbutyl)N(H)-, (1-isopropylbutyl)N(H)-, (1-methylbutyl)N(H)-, (3-methylbutyl)N(H)-, (3,3-dimethylbutyl)N(H)-, (propyl)N(H)-, (butyl)N(H)-, (pentyl)N(H)-, (2-ethyl-3-methylbutyl)N(H)-, (3-methylbut-2-enyl)N(H)-, (cyclobutyl)N(H)-, (cyclopentyl)N(H)-, (cyclohexyl)N(H)-, (cycloheptyl)N(H)-, (thienylmethyl)N(H)-, (furylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (tetrahydronaphthalenyl)N(H)-, and (tetrahydropyranyl)N(H)-, wherein the phenyl, thienyl, thiazolyl, furyl and pyridinyl of (phenylmethyl)O-, phenylCH=N-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (phenylmethyl)N(H)- and (1-phenylethyl)N(H)- are each independently substituted with 0, 1 or 2 susbstituents selected from the group consisting of nitro, cyano, hydroxyl, methoxy, -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, methyl, halo, halomethyl, carboxy, acetyl, and alkyoxycarbonyl.

Exemplary compounds of the fourth embodiment of the present invention of formula (IV) include, but not limited to, the following:

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[(1E)-phenylmethylene]amino}-2(1H)-quinolinone;

1-amino-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2(1H)-quinolinone;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-propoxyquinolin-2(1*H*)-one;

1-(benzylamino)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

1-amino-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(1-propylbutyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(isobutylamino)quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-[(1-ethylpropyl)amino]-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(pentylamino)quinolin-2(1*H*)-one;

1-(cyclohexylamino)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[(2-methyl-1,3-thiazol-4-yl)methyl]amino}quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(isopropylamino)quinolin-2(1*H*)-one;

1-(cyclobutylamino)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

1-(cyclopentylamino)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[3-methylcyclopentyl]amino}quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(tetrahydro-2*H*-pyran-4-ylamino)quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-{[1-ethylbutyl]amino}-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[(3*R*)-3-methylcyclohexyl]amino}quinolin-2(1*H*)-one;

1-(cycloheptylamino)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-{[3-ethylcyclopentyl]amino}-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[1-isopropylbutyl]amino}quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[1-

phenylethyl]amino}quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[1-thien-3-ylethyl]amino}quinolin-2(1*H*)-one;

1-{[3,5-dimethylcyclohexyl]amino}-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(4-isopropylcyclohexyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[1,2,3,4-tetrahydronaphthalen-2-ylamino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[3-(trifluoromethyl)cyclohexyl]amino}quinolin-2(1*H*)-one;

1-(butylamino)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(3-methylbutyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-[(3-furylmethyl)amino]-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-[(2-furylmethyl)amino]-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(thien-2-ylmethyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(1,3-thiazol-2-ylmethyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-{[(2*R*)-2-ethyl-3-methylbutyl]amino}-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(4-methylbenzyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(3-methylbenzyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2-methylbenzyl)amino]quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-{[(3-methylthien-2-yl)methyl]amino}quinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(4-methoxybenzyl)amino]quinolin-2(1*H*)-one;

1-{[(5-chlorothien-2-yl)methyl]amino}-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

1-{[(2-chloro-1,3-thiazol-5-yl)methyl]amino}-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

1-[(3-bromobenzyl)amino]-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

1-[(4-bromobenzyl)amino]-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

1-[(2-bromobenzyl)amino]-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxyquinolin-2(1*H*)-one;

3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(pyridin-3-ylmethyl)amino]quinolin-2(1*H*)-one;

3-({[3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxoquinolin-1(2*H*)-yl]amino}methyl)benzonitrile;

2-({3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

2-({3-[1-(cyclopentylamino)-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

2-({3-[1-(cyclohexylamino)-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

2-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl)oxy]acetamide;

2-({3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4*H*-1,2-benzothiazin-7-yl}oxy)acetamide;

2-({3-[1-(butylamino)-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

2-[(3-{4-hydroxy-1-[(3-methylbutyl)amino]-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl)oxy]acetamide;

3-(8-amino-7-hydroxy-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(isobutylamino)quinolin-2(1*H*)-one;

2-({8-amino-3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

2-({3-[4-hydroxy-2-oxo-1-(propylamino)-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl}oxy)acetamide;

2-({3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl}oxy)propanamide;

2-({3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl}oxy)butanamide;

8-amino-3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-

dioxido-4H-1,2,4-benzothiadiazin-7-yl methanesulfonate;

1-[(cyclopropylmethyl)amino]-4-hydroxy-3-(7-hydroxy-8-nitro-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)quinolin-2(1*H*)-one;

3-(7-{2-[(3*S*)-3-aminopyrrolidin-1-yl]-2-oxoethoxy}-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-1-[(cyclopropylmethyl)amino]-4-hydroxyquinolin-2(1*H*)-one;

2-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl)oxy]-N-ethylacetamide;

[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl)oxy]acetic acid;

3-{7-[2-(3-aminopyrrolidin-1-yl)-2-oxoethoxy]-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl}-1-[(cyclopropylmethyl)amino]-4-hydroxyquinolin-2(1H)-one;

3-(8-amino-7-hydroxy-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-[(cyclopropylmethyl)amino]-4-hydroxyquinolin-2(1H)-one;

2-[(8-amino-3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl)oxy]acetamide;

[(8-amino-3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl)oxy]acetonitrile;

1-[(cyclopropylmethyl)amino]-4-hydroxy-3-[7-(2-hydroxyethoxy)-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl]quinolin-2(1H)-one;

1-[(cyclopropylmethyl)amino]-4-hydroxy-3-[7-(1H-imidazol-2-ylmethoxy)-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl]quinolin-2(1H)-one;

1-[(cyclopropylmethyl)amino]-3-[1,1-dioxido-7-(1,3-thiazol-2-ylmethoxy)-4H-1,2,4-benzothiadiazin-3-yl]-4-hydroxyquinolin-2(1H)-one;

1-[(cyclopropylmethyl)amino]-3-[7-(4,5-dihydro-1H-imidazol-2-ylmethoxy)-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl]-4-hydroxyquinolin-2(1H)-one;

2-{[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl)oxy]methyl}-1,3-thiazole-4-carbonitrile;

3-[7-(2-aminoethoxy)-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl]-1-[(cyclopropylmethyl)amino]-4-hydroxyquinolin-2(1H)-one;

N-{2-[(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl)oxy]ethyl}methanesulfonamide;

3-{7-[(5-bromopyridin-2-yl)oxy]-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl}-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

4-hydroxy-1-(isobutylamino)-3-{7-[(3-nitropyridin-2-yl)oxy]-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl}quinolin-2(1H)-one;

tert-butyl 3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-ylcarbamate;

3-(7-amino-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-[(cyclopropylmethyl)amino]-4-hydroxyquinolin-2(1H)-one;

methyl 2-chloro-6-({3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-1,2,4-benzothiadiazin-7-yl}oxy)isonicotinate;

N-{3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}methanesulfonamide;

N-(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl}-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl)methanesulfonamide;

N-(3-{1-[(cyclopropylmethyl)amino]-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl}-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl)methanesulfonamide;

2-{[3-(1-amino-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl)-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl]oxy}acetamide;

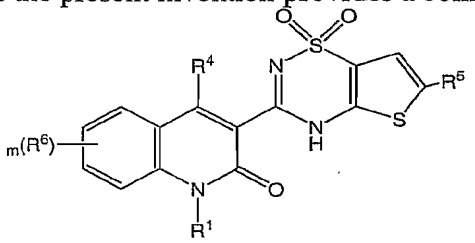
N-{3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}ethanesulfonamide;

benzyl 3-{3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}diazathiane-1-carboxylate 2,2-dioxide;

N-{3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}-*N'*-methylsulfamide; and

N-{3-[1-(cyclobutylamino)-4-hydroxy-2-oxo-1,2-dihydro-3-quinolinyl]-1,1-dioxido-4*H*-1,2,4-benzothiadiazin-7-yl}sulfamide; or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof.

In a fifth embodiment the present invention provides a compound of formula (Va)



(Va)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3

substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, -NH_2, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, R_aR_bNalkyl-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)$alkyl-, $R_aSO_2N(R_f)$alkyl-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)$alkyl-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)$alkyl-, R_kOalkyl-, $R_aR_bNSO_2$-, $R_aR_bNSO_2$alkyl-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. R_kOalkyl-, R_cR_dNalkyl-, R_cR_dNC(O)alkyl-, R_cSO_2-, $R_cSO_2$alkyl-, $R_cC(O)$-, $R_cC(O)$alkyl-, $R_cOC(O)$-, $R_cOC(O)$alkyl-, R_cR_dNalkylC(O)-, R_cR_dNC(O)-, R_cR_dNC(O)Oalkyl-, R_cR_dNC(O)N(R_e)alkyl-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$,

$-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -alkyl$SO_2NR_cR_d$, -alkylC(O)NR_cR_d, $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, $-NR_fR_h$, $-OR_f$, $-CO(R_f)$, $-SR_f$, $-SOR_f$, $-SO_2R_f$, $-C(O)NR_fR_h$, $-SO_2NR_fR_h$, $-C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), $-SR_f$, $-S(O)R_f$, $-S(O)_2R_f$, $-OR_f$, $-N(R_f)(R_h)$, $-C(O)R_f$, $-C(O)OR_f$, $-C(O)NR_fR_h$, $-C(O)N(H)NR_fR_h$, $-N(R_e)C(O)OR_f$, $-N(R_e)SO_2NR_fR_h$, $-N(R_e)C(O)NR_fR_h$, -alkyl$N(R_e)C(O)OR_f$, -alkyl$N(R_e)SO_2NR_fR_h$, and -alkyl$N(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), $-SR_f$, $-S(O)R_f$, $-S(O)_2R_f$, $-OR_f$, $-N(R_f)(R_h)$, $-C(O)R_f$, $-C(O)OR_f$ and $-C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), $-SO_2$alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl),

-C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkylN(alkyl)$_2$, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, R_aS(O)-, R_aSO_2-, R_aSalkyl-, R_a(O)Salkyl-, $R_aSO_2$alkyl-, R_aOC(O)-, R_aOC(O)alkyl-, R_aC(O)-, R_aC(O)alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d; and

m is 0, 1, 2, 3, or 4;

with the proviso that when R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, R_aC(O)-, R_aS-, R_a(O)S-, $R_a(O)_2$S-, R_aSO_2N(R_f)-, R_aR_bNC(O)-, R_kOC(O)-, R_aR_bNSO_2- or -OR_k, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR_a, -S(O)R_a, -$S(O)_2R_a$, -OR_k, -N(R_a)(R_b), -C(O)R_a, -C(O)OR_a and -C(O)NR_aR_b, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (Va) wherein R^4 is hydroxy.

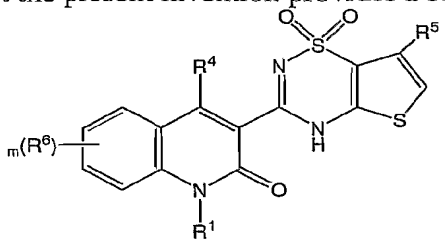
For example, the present invention provides a compound of formula (Va) wherein R^4 is hydroxy and wherein R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl,

formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, R_fR_gC=N- and R_kO-.

For example, the present invention provides a compound of formula (Va) wherein R^4 is hydroxy and wherein R^1 is selected from the group consisting of C1-C7 alkyl, phenyl-C1-C2 alkyl-, heteroaryl-C1-C2 alkyl-, ((C3-C6 cycloalkyl) C1-C2 alkyl)-,(C1-C7 alkyl)O-, (C3-C7 cycloalkyl)O-, phenyl-C1-C2 alkyl-O-, $-NH_2$, (C1-C7 alkyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)C1-C2 alkyl)N(H)-, (heterocycle)N(H)-, (heteroarylalkyl)N(H)-,(arylalkyl)N(H)-.

For example, the present invention provides a compound of formula (Va) wherein R^4 is hydroxy and wherein R^1 is selected from the group consisting of isopropyl, 3-methylbutyl, butyl, isobutyl, phenylmethyl, thienylmethyl, cyclobutylmethyl, cyclopropylethyl, $-NH_2$, (isopropyl)N(H)-, (isobutyl)N(H)-, (3-methylbutyl)N(H)-, (cyclobutyl)N(H)- and (cyclopropylmethyl)N(H)-; wherein the phenylmethyl and the thienylmethyl are independently unsubstituted or substituted with 1, 2 or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, halo, cyano, nitro, $-NH_2$, -N(H)alkyl, --N(alkyl)$_2$, hydroxy and alkoxy.

In a sixth embodiment the present invention provides a compound of formula (Vb)



(Vb)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, R_fR_gC=N- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_e)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and $-OR_k$, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, $-OR_a$, $-NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$ and $-NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2

or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -alkyl$SO_2NR_cR_d$, -alkyl$C(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -alkyl$N(R_e)C(O)OR_f$, -alkyl$N(R_e)SO_2NR_fR_h$, and -alkyl$N(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)$C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -$C(O)NH_2$, -$C(O)NH_2$, -C(O)N(H)(alkyl), and -$C(O)N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, $-alkylNH_2$, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), $-alkylSO_2alkyl$, $-alkylN(alkyl)_2$, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bNalkyl$-, $R_aOalkyl$-, $R_aR_bNC(O)$-, $R_aR_bNC(O)alkyl$, R_aS-, $R_aS(O)$-, R_aSO_2-, $R_aSalkyl$-, $R_a(O)Salkyl$-, R_aSO_2alkyl-, $R_aOC(O)$-, $R_aOC(O)alkyl$-, $R_aC(O)$-, $R_aC(O)alkyl$-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$; and

m is 0, 1, 2, 3, or 4;

with the proviso that when R^4 is hydroxy or R_eS-, and R^5 is hydrogen, unsubstituted alkyl, halo or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (Vb) wherein R^4 is hydroxy.

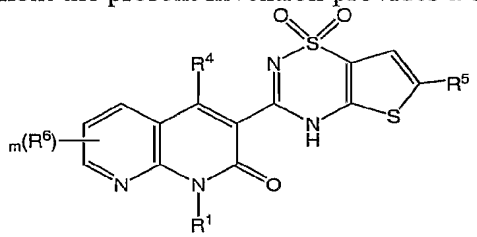
For example, the present invention provides a compound of formula (Vb) wherein R^4 is hydroxyl and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, $R_aR_bNalkyl$-, $R_aR_bNC(O)alkyl$-, $R_fR_gC{=}N$- and R_kO-.

For example, the present invention provides a compound of formula (Vb) wherein R^4 is hydroxy and wherein R^1 is selected from the group consisting of C1-C7 alkyl, phenyl-C1-C2 alkyl-, heteroaryl-C1-C2 alkyl-, ((C3-C6 cycloalkyl) C1-C2 alkyl)-,(C1-C7 alkyl)O-, (C3-

C7 cycloalkyl)O-, phenyl-C1-C2 alkyl-O-, $-NH_2$, (C1-C7 alkyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)C1-C2 alkyl)N(H)-, (heterocycle)N(H)-, (heteroarylalkyl)N(H)-,(arylalkyl)N(H)-.

For example, the present invention provides a compound of formula (Vb) wherein R^4 is hydroxy and wherein R^1 is selected from the group consisting of isopropyl, 3-methylbutyl, butyl, isobutyl, phenylmethyl, thienylmethyl, cyclobutylmethyl, cyclopropylethyl, $-NH_2$, (isopropyl)N(H)-, (isobutyl)N(H)-, (3-methylbutyl)N(H)-, (cyclobutyl)N(H)- and (cyclopropylmethyl)N(H)-; wherein the phenylmethyl and the thienylmethyl are independently unsubstituted or substituted with 1, 2 or 3 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, haloalkyl, halo, cyano, nitro, $-NH_2$, -N(H)alkyl, --N(alkyl)$_2$, hydroxy and alkoxy.

In a seventh embodiment the present invention provides a compound of formula (VIa)



(VIa)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, R_fR_gC=N- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_e)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo,

haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and $-OR_k$, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, $-OR_a$, $-NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$ and $-NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-alkylSO_2NR_cR_d$, $-alkylC(O)NR_cR_d$, $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting

of hydrogen, $-NR_fR_h$, $-OR_f$, $-CO(R_f)$, $-SR_f$, $-SOR_f$, $-SO_2R_f$, $-C(O)NR_fR_h$, $-SO_2NR_fR_h$, $-C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), $-SR_f$, $-S(O)R_f$, $-S(O)_2R_f$, $-OR_f$, $-N(R_f)(R_h)$, $-C(O)R_f$, $-C(O)OR_f$, $-C(O)NR_fR_h$, $-C(O)N(H)NR_fR_h$, $-N(R_e)C(O)OR_f$, $-N(R_e)SO_2NR_fR_h$, $-N(R_e)C(O)NR_fR_h$, -alkylN(R_e)C(O)OR_f, -alkylN(R_e)$SO_2NR_fR_h$, and -alkylN(R_e)C(O)NR_fR_h;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), $-SR_f$, $-S(O)R_f$, $-S(O)_2R_f$, $-OR_f$, $-N(R_f)(R_h)$, $-C(O)R_f$, $-C(O)OR_f$ and $-C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), $-SO_2$alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylN$(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N$(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl),

-S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH$_2$, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO$_2$alkyl, -alkylN(alkyl)$_2$, -N(H)C(O)NH$_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH$_2$, -C(O)NH$_2$, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, R_aS(O)-, R_aSO$_2$-, R_aSalkyl-, R_a(O)Salkyl-, R_aSO$_2$alkyl-, R_aOC(O)-, R_aOC(O)alkyl-, R_aC(O)-, R_aC(O)alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR$_c$), -(alkyl)(NR$_c$R$_d$), -SR$_c$, -S(O)R$_c$, -S(O)$_2$R$_c$, -OR$_c$, -N(R$_c$)(R$_d$), -C(O)R$_c$, -C(O)OR$_c$ and -C(O)NR$_c$R$_d$; and

m is 0, 1, 2, 3, or 4;

with the proviso that R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, R_aC(O)-, R_aS-, R_a(O)S-, R_a(O)$_2$S-, R_aSO$_2$N(R$_f$)-, R_aR_bNC(O)-, R_kOC(O)-, R_aR_bNSO$_2$- or -OR$_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR$_a$, -S(O)R$_a$, -S(O)$_2$R$_a$, -OR$_k$, -N(R$_a$)(R$_b$), -C(O)R$_a$, -C(O)OR$_a$ and -C(O)NR$_a$R$_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a comound of formula (VIa) wherein R^4 is hydroxy.

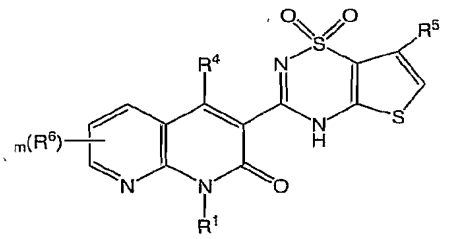
For example, the present invention provides a comound of formula (VIa) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, R_aR_bNalkyl-, R_aR_bNC(O)alkyl-, R_fR_gC=N- and R_kO-.

For example, the present invention provides a compound of formula (VIa) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, C1-C7 alkyl, C1-C6 alkenyl, (C3-C7 cycloalkyl)(C1-C2 alkyl)-, (C5-C6 cycloalkenyl)(C1-C2 alkyl)-, C3-C7 cycloalkyl, phenyl-C1-C2 alkyl-, furyl(C1-C2 alkyl)-, thienyl(C1-C2 alkyl)-, phenyl(C1-C2 alkyl)-, pyridinyl(C1-C2 alkyl)-, thiazolyl(C1-C2 alkyl)-, isoxazolyl(C1-C2alkyl)-, naphthyl(C1-C2 alkyl), benzothienyl(C1-C2 alkyl)-, indolyl(C1-C2 alkyl)-, phenylN(H)(C1-C6 alkyl)-, (C1-C7 alkyl)O-, (C3-C6 cycloalkyl)O-, ((phenyl)C1-C2 alkyl)O-, phenylCH=N-,

NH_2, (C1-C7 alkyl)N(H)-, (C1-C7 alkenyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)C1-C2 alkyl)N(H)-, ((phenyl)C1-C2 alkyl)N(H)-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (tetrahydropyran)N(H)-, (benzyl)N(H)-, (tetrahydronaphthalenyl)N(H)-, wherein each R^1 is substituted with 0, 1, 2, or 3 substituents selected from the group consisting of alkyl, hydroxy, oxo, halo, cyano, nitro, haloalkyl, hydroxyl, alkoxy, haloalkoxy, phenyl, piperazinyl, morphilinyl, carboxy, -C(O)O(alkyl), $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -Oalkyl, -O-phenyl.

For example, the present invention provides a comound of formula (VIa) wherein R^4 is hydroxy and R^1 is selected from the group consisting of phenylmethyl, phenylethyl, C3 alkyl, C4 alkyl, C5 alkyl, cyclopropylmethyl, cyclopropylethyl, cyclobutylmethyl, (5-chloro-thien-2-yl)methyl- (C3 alkyl)N(H)-, (C4 alkyl)N(H)-, (C5 alkyl)N(H)-, (cyclobutyl)N(H)- and (cyclopropylmethyl)N(H)-.

In an eighth embodiment the the present invention provides a compound of formula (VIb)



(VIb)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_e), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_e;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –

COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$,

-alkylC(O)NR_cR_d, -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -C(O)NR_fR_h, -$SO_2NR_fR_h$, -C(O)OR_f, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -C(O)R_f, -C(O)OR_f, -C(O)NR_fR_h, -C(O)N(H)NR_fR_h, -$N(R_e)$C(O)OR_f, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)$C(O)NR_fR_h, -alkyl$N(R_e)$C(O)OR_f, -alkyl$N(R_e)SO_2NR_fR_h$, and -alkyl$N(R_e)$C(O)NR_fR_h;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -C(O)R_f, -C(O)OR_f and -C(O)NR_fR_h;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)$N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with

0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, $-alkylNH_2$, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), $-alkylSO_2alkyl$, $-alkylN(alkyl)_2$, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bNalkyl$-, $R_aOalkyl$-, $R_aR_bNC(O)$-, $R_aR_bNC(O)alkyl$, R_aS-, $R_aS(O)$-, R_aSO_2-, $R_aSalkyl$-, $R_a(O)Salkyl$-, R_aSO_2alkyl-, $R_aOC(O)$-, $R_aOC(O)alkyl$-, $R_aC(O)$-, $R_aC(O)alkyl$-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$; and

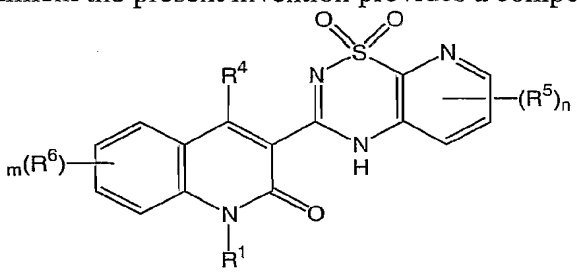
m is 0, 1, 2, 3, or 4;

with the proviso that when R^4 is hydroxy or R_eS-, and R^5 is hydrogen, unsubstituted alkyl, halo or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (VIb) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, C1-C7 alkyl, C1-C6 alkenyl, (C3-C7 cycloalkyl)(C1-C2 alkyl)-, (C5-C6 cycloalkenyl)(C1-C2 alkyl)-, C3-C7 cycloalkyl, phenyl-C1-C2 alkyl-, furyl(C1-C2 alkyl)-, thienyl(C1-C2 alkyl)-, phenyl(C1-C2 alkyl)-, pyridinyl(C1-C2 alkyl)-, thiazolyl(C1-C2 alkyl)-, isoxazolyl(C1-C2alkyl)-, naphthyl(C1-C2 alkyl), benzothienyl(C1-C2 alkyl)-, indolyl(C1-C2 alkyl)-, phenylN(H)(C1-C6 alkyl)-, (C1-C7 alkyl)O-, (C3-C6 cycloalkyl)O-, ((phenyl)C1-C2 alkyl)O-, phenylCH=N-, NH_2, (C1-C7 alkyl)N(H)-, (C1-C7 alkenyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)C1-C2 alkyl)N(H)-, ((phenyl)C1-C2 alkyl)N(H)-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (tetrahydropyran)N(H)-, (benzyl)N(H)-, (tetrahydronaphthalenyl)N(H)-, wherein each R^1 is substituted with 0, 1, 2, or 3 substituents selected from the group consisting of alkyl, hydroxy, oxo, halo, cyano, nitro, haloalkyl, hydroxyl, alkoxy, haloalkoxy, phenyl, piperazinyl, morphilinyl, carboxy, -C(O)O(alkyl), $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -Oalkyl, -O-phenyl.

For example, the present invention provides a comound of formula (VIb) wherein R^4 is hydroxy and R^1 is selected from the group consisting of phenylmethyl, phenylethyl, C3 alkyl, C4 alkyl, C5 alkyl, cyclopropylmethyl, cyclopropylethyl, cyclobutylmethyl, (5-chloro-thien-2-yl)methyl- (C3 alkyl)N(H)-, (C4 alkyl)N(H)-, (C5 alkyl)N(H)-, (cyclobutyl)N(H)- and (cyclopropylmethyl)N(H)-.

In a ninth embodiment the present invention provides a compound of formula (VII)



(VII)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, -NH_2, and -COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, R_aR_bNalkyl-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)$alkyl-, $R_aSO_2N(R_f)$alkyl-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)$alkyl-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)$alkyl-, R_kOalkyl-, $R_aR_bNSO_2$-, $R_aR_bNSO_2$alkyl-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is

independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$, -$alkylC(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo,

halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -alkyl$N(R_e)C(O)OR_f$, -alkyl$N(R_e)SO_2NR_fR_h$, and -alkyl$N(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)$C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -$C(O)NH_2$, -$C(O)NH_2$, -C(O)N(H)(alkyl), and -$C(O)N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkyl$N(alkyl)_2$, -N(H)$C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -$C(O)NH_2$, -$C(O)NH_2$, -C(O)N(H)(alkyl), and -$C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl,

haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bN$alkyl-, R_aOalkyl-, $R_aR_bNC(O)$-, $R_aR_bNC(O)$alkyl, R_aS-, $R_aS(O)$-, R_aSO_2-, R_aSalkyl-, $R_a(O)$Salkyl-, $R_aSO_2$alkyl-, $R_aOC(O)$-, $R_aOC(O)$alkyl-, $R_aC(O)$-, $R_aC(O)$alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

m is 0, 1, 2, 3, or 4; and

n is 0, 1, 2, 3 or 4;

with the proviso that when R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or -OR_k, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl.

For example, the present invention provides a compound of formula (VII) wherein R^4 is hydroxy.

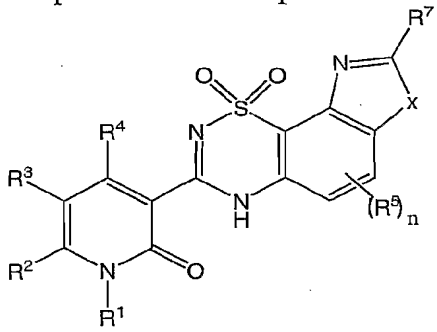
For example, the present invention provides a compound of formula (VII) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, R_fR_gC=N- and R_kO-.

For example, the present invention provides a compound of formula (VII) wherein R^4 is hydroxy and R^1 is selected from the group consisting of hydrogen, C1-C7 alkyl, C1-C6 alkenyl, furyl(C1-C2 alkyl)-, thienyl(C1-C2 alkyl)-, phenyl(C1-C2 alkyl)-, pyridinyl(C1-C2 alkyl)-, thiazolyl(C1-C2 alkyl)-, isoxazolyl(C1-C2alkyl)-, naphthyl(C1-C2 alkyl), benzothienyl(C1-C2 alkyl)-, indolyl(C1-C2 alkyl)-, (C3-C7 cycloalkyl)(C1-C2 alkyl)-, (C5-C6 cycloalkenyl)(C1-C2 alkyl)-, C3-C7 cycloalkyl, phenylN(H)(C1-C6 alkyl)-, (phenylalkyl)O-, (C1-C7 alkyl)O-, (C3-C6 cycloalkyl)O-, phenylCH=N-, NH_2, (C1-C7 alkyl)N(H)-, (C1-C7 alkenyl)N(H)-, (C3-C7 cycloalkyl)N(H)-, ((C3-C7 cycloalkyl)C1-C2 alkyl)N(H)-, (thienylmethyl)N(H)-, (thiazolylmethyl)N(H)-, (furylmethyl)N(H)-, (pyridinylmethyl)N(H)-, (tetrahydropyran)N(H)-, (phenylalkyl)N(H)-, (tetrahydronaphthalenyl)N(H)-, wherein each R^1 is substituted with 0, 1, 2, or 3 substituents

selected from the group consisting of alkyl, hydroxy, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, phenyl, piperazinyl, morphilinyl, carboxy, -C(O)O(alkyl), $-NH_2$, -NH(alkyl), $-N(alkyl)_2$, -Oalkyl, -O-phenyl.

For example, the present invention provides a compound of formula (VII) wherein R^4 is hydroxy and R^1 is selected from the group consisting of C3 alkyl, C4 alkyl, C5 alkyl, phenylmethyl, (5-chloro-thien-2-yl)methyl-, $-NH_2$, (C3 alkyl)N(H)-, (C4 alkyl)N(H)-, (C5 alkyl)N(H)-, (cyclobutyl)N(H)- and (cyclopropylmethyl)N(H)-.

In a tenth embodiment the present invention provides a compound of formula (VIII)



(VIII)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

X is NH, N(alkyl), O or S;

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_e)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_e$;

R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, $-N(R_a)(R_b)$, $R_aR_bNC(O)$-, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$ and $R_aC(O)$-; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$;

alternatively, R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is independently substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and $-OR_k$, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, $-(alkyl)(OR_c)$, $-(alkyl)(NR_cR_d)$, $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, $-(alkyl)(OR_k)$, $-(alkyl)(NR_aR_b)$, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, $-OR_a$, $-NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$ and $-NC(O)R_a$;

R^7 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$-, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and $-OR_k$, wherein each R^7 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, $-(alkyl)(OR_c)$,

-(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$, -$alkylC(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -$alkylN(R_e)C(O)OR_f$, -$alkylN(R_e)SO_2NR_fR_h$, and -$alkylN(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl,

heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -N(R_f)(R_h), -C(O)R_f, -C(O)OR_f and -C(O)NR_fR_h;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylN(alkyl)$_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkylN(alkyl)$_2$, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, R_aS(O)-, R_aSO_2-, R_aSalkyl-, R_a(O)Salkyl-, $R_aSO_2$alkyl-, R_aOC(O)-, R_aOC(O)alkyl-, R_aC(O)-, R_aC(O)alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

m is 0, 1, 2, 3, or 4; and

n is 0, 1 or 2.

For example, the present invention provides a compound of formula (VIII) wherein

R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$.

For example, the present invention provides a compound of formula (VIII) wherein R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazolyl, cyclopentyl, cyclohexyl and thienyl.

For example, the present invention provides a compound of formula (VIII) wherein R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazolyl, cyclopentyl, cyclohexyl and thienyl and R^4 is hydroxy.

For example, the present invention provides a compound of formula (VIII) wherein R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazolyl, cyclopentyl, cyclohexyl and thienyl, R^4 is hydroxy, and R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkynyl, arylalkenyl, arylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, R_aR_bN-, $R_aR_bNalkyl$-, $R_aR_bNC(O)alkyl$-, $R_fR_gC=N$- and R_kO-.

For example, the present invention provides a compound of formula (VIII) wherein R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazolyl, cyclopentyl, cyclohexyl and thienyl, R^4 is hydroxy, and R^1 is selected from the group consisting of C1-C7 alkyl, (C3-C6 cycloalkyl)C1-C2 alkyl)-, phenyl-C1-C2 alkyl-, heteroaryl-C1-C2 alkyl-, ((phenyl)C1-C2 alkyl)O-, (C3-C7 alkyl)O-, (C3-C6 cycloalkyl)O-, ((phen;yl)C1-C2 alkyl)N(H)-, (C3-C6 cycloalkyl)N(H)-, ((C3-C6 cycloalkyl)C1-C2 alkyl)N(H)- and (C1-C7 alkyl)N(H)-.

For example, the present invention provides a compound of formula (VIII) wherein R^2 and R^3, together with the carbon atoms to which they are attached, form a five- or six-membered ring selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyridazinyl, pyrazolyl, cyclopentyl, cyclohexyl and thienyl, R^4 is hydroxy, and R^1 is selected from the group consisting of C3 alkyl, C4 alkyl, C5 alkyl, phenylmethyl, phenylethyl, (5-chloro-thien-2-yl)methyl, cyclobutylmethyl, cyclopropylmethyl, cyclopropylethyl, (cyclopropylmethyl)N(H)-, (cyclobutyl)N(H)-, (cyclopentyl)N(H)-, (cyclohexyl)N(H)-, (phenylmethyl)N(H)-, (C3 alkyl)N(H)-, (C4 alkyl)N(H)- and (C5 alkyl)N(H)-.

Exemplary compounds of the tenth embodiment of the present invention of formula (VIII) include, but not limited to, the following:

3-(1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl)-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

3-[8-(chloromethyl)-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

3-{3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-8-yl}propanoic acid;

3-(8-{[(2-aminoethyl)amino]methyl}-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl)-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

methyl {3-[4-hydroxy-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-3-yl]-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-8-yl}acetate;

4-hydroxy-3-(8-{[(3R)-3-hydroxypyrrolidin-1-yl]methyl}-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl)-1-(isobutylamino)quinolin-2(1H)-one;

3-[1,1-dioxido-8-(pyridinium-1-ylmethyl)-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl]-1-(isobutylamino)-2-oxo-1,2-dihydroquinolin-4-olate;

3-[1,1-dioxido-8-(pyrrolidin-1-ylmethyl)-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

3-[8-(3-aminophenyl)-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

3-[8-(aminomethyl)-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

4-hydroxy-3-[8-(hydroxymethyl)-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl]-1-(isobutylamino)quinolin-2(1H)-one;

3-{8-[(butylamino)methyl]-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl}-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

3-[9-(butylamino)-1,1-dioxido-4H,8H-[1,4]oxazino[2,3-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(isobutylamino)quinolin-2(1H)-one;

4-hydroxy-1-(3-methylbutyl)-3-(8-methyl-1,1-dioxido-4H-[1,3]oxazolo[5,4-h][1,2,4]benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

3-[1,1-dioxido-8-(trifluoromethyl)-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one;

4-hydroxy-3-(8-hydroxy-1,1-dioxido-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-3-yl)-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one;

4-hydroxy-1-(3-methylbutyl)-3-(8-methyl-1,1-dioxido-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one;

3-[1,1-dioxido-8-(pentafluoroethyl)-4,7-dihydroimidazo[4,5-

h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one;

3-[8-(chloromethyl)-1,1-dioxido-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-3-yl]-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one;

{3-[4-hydroxy-1-(3-methylbutyl)-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl]-1,1-dioxido-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-8-yl}acetonitrile;

methyl {3-[4-hydroxy-1-(3-methylbutyl)-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl]-1,1-dioxido-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-8-yl}acetate;

3-(9,9-dioxido-6*H*-[1,2,5]thiadiazolo[3,4-*h*][1,2,4]benzothiadiazin-7-yl)-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1*H*)-one;

3-(8-amino-1,1-dioxido-4,7-dihydroimidazo[4,5-h][1,2,4]benzothiadiazin-3-yl)-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one; and

4-hydroxy-3-[8-(hydroxymethyl)-1,1-dioxido-4,9-dihydroimidazo[4,5-*h*][1,2,4]benzothiadiazin-3-yl]-1-(3-methylbutyl)-1,8-naphthyridin-2(1*H*)-one, or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof.

In an eleventh embodiment the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, and a pharmaceutically acceptable carrier.

In a twelfth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, with one or more host immune modulators, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (V), (VI), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, with one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and a pharmaceutically acceptable carrier.

In a thirteenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, with one or more second antiviral agents, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds

of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, with one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, with one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, and a pharmaceutically acceptable carrier.

In a fourteenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising, a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral

genome, and a pharmaceutically acceptable carrier.

In a fifteenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a sixteenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a seventeenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of

compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In an eighteenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a nineteenth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically

acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

In a twentieth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

In a twenty-first embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically

acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

Preferably, the agent that treat patients for disease caused by hepatitis B(HBV) infection in the above mentioned pharmaceutical compositions can be selected from the group consisting of L-deoxythymidine, adefovir, lamivudine and tenfovir.

In a twenty-second embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a twenty-third embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV)

infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a twenty-fourth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a twenty-fifth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds

of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a twenty-sixth embodiment, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV), and a pharmaceutically acceptable carrier.

For example, the present invention provides a pharmaceutical composition comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

The agent that treats patients for disease caused by human immunodeficiency virus (HIV) infection in the above-mentioned pharmaceutical compositions may be, for example but not limited thereto, ritonavir, lopinavir, indinavir, nelfinavir, saquinavir, amprenavir, atazanavir, tipranavir, TMC-114, fosamprenavir, zidovudine, lamivudine, didanosine, stavudine, tenofovir, zalcitabine, abacavir, efavirenz, nevirapine, delavirdine, TMC-125, L-870812, S-1360, enfuvirtide (T-20) or T-1249, or any combination thereof.

In a twenty-seventh embodiment, the present invention provides a method of treating or preventing infection caused by an RNA-containing virus comprising administering to a patient in need of such treatment any one of the pharmaceutical compositions disclosed hereinabove.

In a twenty-eighth embodiment, the present invention provides a method of inhibiting the replication of an RNA-containing virus comprising contacting said virus with a

therapeuctially effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt thereof.

In a twenty-ninth embodiment, the present invention provides a method of treating or preventing infection caused by an RNA-containing virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt thereof.

For example, the present invention provides a method of treating or preventing infection caused by an RNA-containing virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt thereof wherein theRNA-containing virus is hepatitis C virus.

In a thirtieth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) and one or more host immune modulators.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) and one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant.

In a thirty-first embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) and one or more second antiviral agents.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) and one or more second antiviral agents which inhibit replication of HCV by inhibiting host cellular functions associated with viral replication.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) and one or more second antiviral agents which inhibit replication of HCV by targeting proteins of the viral genome.

In a thirty-second embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) one or more host immune modulators, and one or more second antiviral agents.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more second antiviral agents.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more second antiviral agents which inhibit replication of HCV by inhibiting host cellular functions associated with viral replication.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more second antiviral agents which inhibit replication of HCV by targeting proteins of the viral genome.

In a thirty-third embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a

pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a thirty-fourth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a thirty-fifth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in

pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a thirty-fourth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a thirty-fifth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in

need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, and a pharmaceutically acceptable carrier.

In a thirty-sixth embodiment, the present invention a method of treating or preventing

infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

In a thirty-seventh embodiment, the present invention a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

In a thirty-eighth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing

infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

In a thirty-ninth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group

consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, and a pharmaceutically acceptable carrier.

An agent that treats patients for disease caused by hepatitis B (HBV) infection may be, for example but not limited thereto, L-deoxythymidine, adefovir, lamivudine or tenfovir, or any combination thereof.

In a fortieth embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a forty-first embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a forty-second embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV)

infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen comprising a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

In a forty-third embodiment, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically

acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV), and a pharmaceutically acceptable carrier.

For example, the present invention provides a method of treating or preventing infection caused by an hepatitis C virus comprising administering to a patient in need of such treatmen a therapeutically effective amount of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, and a pharmaceutically acceptable carrier.

An agent that treats patients for disease caused by human immunodeficiency virus (HIV) infection may be, for example but not limited thereto, ritonavir, lopinavir, indinavir, nelfinavir, saquinavir, amprenavir, atazanavir, tipranavir, TMC-114, fosamprenavir, zidovudine, lamivudine, didanosine, stavudine, tenofovir, zalcitabine, abacavir, efavirenz, nevirapine, delavirdine, TMC-125, L-870812, S-1360, enfuvirtide (T-20) or T-1249, or any combination thereof.

In a forty-fourth embodiment the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, to prepare a medicament for treating or preventing infection caused by an RNA-containing virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, to prepare a medicament for treating or preventing infection caused by an RNA-containing virus in a patient, wherein the RNA-containing virus is hepatitis C virus.

In a forty-fifth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, and one or more host immune modulators, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of

compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, and one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a forty-sixth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, and one or more second antiviral agents, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, and one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, and one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a forty-seventh embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, one or more host immune modulators, and one or more second antiviral agents, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more second antiviral agents, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, one or more host immune modulators selected from

the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more second antiviral agents which inhibit replication of HCV by inhibiting host cellular functions associated with viral replication, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more second antiviral agents which inhibit replication of HCV by targeting proteins of the viral genome, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a forty-eighth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a therapeutically acceptable salt thereof, one or more host immune modulators, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a forty-ninth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral

replication, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fiftieth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In another preferred embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a

pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by targeting proteins of the viral genome, and one or more agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of liver, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-first embodiment, the present invention a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-second embodiment, the present invention a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-third embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and one or more agents that treat patients for disease caused by hepatitis B

(HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-fourth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by

targeting proteins of the viral genome, and one or more agents that treat patients for disease caused by hepatitis B (HBV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

An agent that treats patients for disease caused by hepatitis B (HBV) infection may be, for example but not limited thereto, L-deoxythymidine, adefovir, lamivudine or tenfovir, or any combination thereof.

In a fifty-fifth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-sixth embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-seventh embodiment, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing

infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more second antiviral agents which inhibit the replication of HCV by targeting proteins of the viral genome, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

In a fifty-eighth embodiment, the present invention provides a use of compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators, one or more second antiviral agents, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

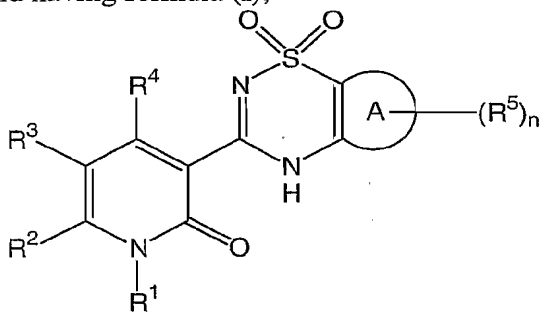
For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which inhibit the replication of HCV by inhibiting host cellular functions associated with viral replication, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV), to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

For example, the present invention provides a use of a compound or combination of compounds of formula (I), (II), (III), (IV), (Va), (Vb), (VIa), (VIb), (VII) or (VIII), or a pharmaceutically acceptable salt form thereof, one or more host immune modulators selected from the group consisting of interferon-alpha, pegylated-interferon-alpha, interferon-beta, interferon-gamma, a cytokine, a vaccine and a vaccine comprising an antigen and an adjuvant, one or more second antiviral agents which which inhibit the replication of HCV by

targeting proteins of the viral genome, and one or more agents that treat patients for disease caused by human immunodeficiency virus (HIV) infection, to prepare a medicament for treating or preventing infection caused by an hepatitis C virus in a patient.

An agent that treats patients for disease caused by human immunodeficiency virus (HIV) infection may be, for example but not limited thereto, ritonavir, lopinavir, indinavir, nelfinavir, saquinavir, amprenavir, atazanavir, tipranavir, TMC-114, fosamprenavir, zidovudine, lamivudine, didanosine, stavudine, tenofovir, zalcitabine, abacavir, efavirenz, nevirapine, delavirdine, TMC-125, L-870812, S-1360, enfuvirtide (T-20) or T-1249, or anycombination thereof.

In a fifty-ninth embodiment, the present invention provides a process for the preparation of a compound having formula (I),



(I)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

A is a monocyclic or bicyclic ring selected from the group consisting of aryl, cycloalkyl, cycloalkenyl, heteroaryl and heterocycle;

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bNalkyl$-, $R_aR_bNC(O)alkyl$-, $R_aR_bNC(O)Oalkyl$-, $R_aR_bNC(O)NR_calkyl$-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, -$N(R_a)(R_b)$, $R_aR_bNC(O)$-, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$ and $R_aC(O)$-;

wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$;

alternatively, R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is independently substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH, $-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, R_aR_bNalkyl-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)$alkyl-, $R_aSO_2N(R_f)$alkyl-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)$alkyl-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)$alkyl-, R_kOalkyl-, $R_aR_bNSO_2$-, $R_aR_bNSO_2$alkyl-, $(R_bO)(R_a)P(O)O$- and -OR_k, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. R_kOalkyl-, R_cR_dNalkyl-, R_cR_dNC(O)alkyl-, R_cSO_2-, $R_cSO_2$alkyl-, $R_cC(O)$-, $R_cC(O)$alkyl-, $R_cOC(O)$-, $R_cOC(O)$alkyl-,

$R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -$alkylSO_2NR_cR_d$, -$alkylC(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -$alkylN(R_e)C(O)OR_f$, -$alkylN(R_e)SO_2NR_fR_h$, and -$alkylN(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl,

cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylN(alkyl)$_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

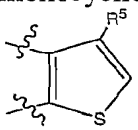
alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -N(alkyl)$_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -alkylN(alkyl)$_2$, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)N(alkyl)$_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, R_aR_bNalkyl-, R_aOalkyl-, R_aR_bNC(O)-, R_aR_bNC(O)alkyl, R_aS-, R_aS(O)-, R_aSO_2-, R_aSalkyl-, R_a(O)Salkyl-, $R_aSO_2$alkyl-, R_aOC(O)-, R_aOC(O)alkyl-, R_aC(O)-, R_aC(O)alkyl-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -N(R_c)(R_d), -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

m is 0, 1, 2, 3, or 4; and

n is 0, 1, 2, 3, or 4;

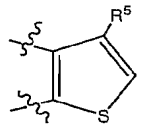
with the proviso that when A is a monocyclic ring other than



and R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or -OR_k, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, -SR_a, -S(O)R_a, -$S(O)_2R_a$, -OR_k, -N(R_a)(R_b), -C(O)R_a, -C(O)OR_a and -C(O)NR_aR_b, then R^1 is

not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl;

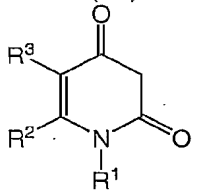
and with the further proviso that when A is



and R^4 is hydroxy or R_eS-, and R^5 is hydrogen, unsubstituted alkyl, halo or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl;

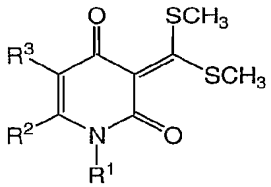
comprising:

(a) contacting a compound of formula (26)



(26)

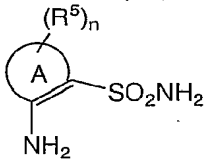
with carbon disulfide and a methylating agent in the presence of a base to provide a compound of formula (27)



(27);

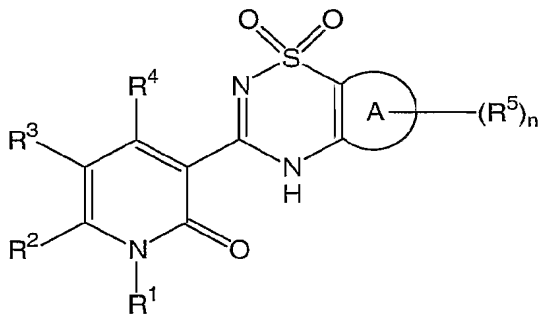
and

(b) contacting the compound of formula (27) with a compound of formula (13)



(13).

In a sixtieth embodiment the present invention provides a process for the preparation of a compound having formula (I),



(I)

or a pharmaceutically acceptable salt form, stereoisomer or tautomer thereof, wherein:

A is a monocyclic or bicyclic ring selected from the group consisting of aryl, cycloalkyl, cycloalkenyl, heteroaryl and heterocycle;

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, $R_fR_gC{=}N$- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, -$N(R_a)(R_b)$, $R_aR_bNC(O)$-, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$ and $R_aC(O)$-; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$;

alternatively, R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$;

R^4 is selected from the group consisting of alkoxy, arylalkoxy, aryloxy, halo, hydroxy, R_aR_bN-, N_3-, R_eS-, wherein R^4 is independently substituted with 0, 1 or 2 substituents independently selected from the group consisting of halo, nitro, cyano, -OH,

$-NH_2$, and –COOH;

R^5 is independently selected at each occurrence from the group consisting of alkenyl, alkoxy, alkyl, alkynyl, aryl, arylalkyl, arylcarbonyl, aryloxy, azidoalkyl, formyl, halo, haloalkyl, halocarbonyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydoxyalkyl, cycloalkyl, cyano, cyanoalkyl, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aR_bNalkyl$-, $R_a(O)SN(R_f)$-, $R_aSO_2N(R_f)$-, $R_a(O)SN(R_f)alkyl$-, $R_aSO_2N(R_f)alkyl$-, $R_aR_bNSO_2N(R_f)$-, $R_aR_bNSO_2N(R_f)alkyl$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_kOC(O)alkyl$-, $R_kOalkyl$, $R_aR_bNSO_2$-, $R_aR_bNSO_2alkyl$-, $(R_bO)(R_a)P(O)O$- and $-OR_k$, wherein each R^5 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, $-OR_a$, $-NR_aR_b$, $-SR_a$, $-SOR_a$, $-SO_2R_a$, $-C(O)OR_a$, $-C(O)NR_aR_b$ and $-NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-. $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -alkyl$SO_2NR_cR_d$,

-alkylC(O)NR_cR_d, -SR_c, -S(O)R_c, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -C(O)R_c, -C(O)OR_c and -C(O)NR_cR_d;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -C(O)NR_fR_h, -$SO_2NR_fR_h$, -C(O)OR_f, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -C(O)R_f, -C(O)OR_f, -C(O)NR_fR_h, -C(O)N(H)NR_fR_h, -$N(R_e)$C(O)OR_f, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)$C(O)NR_fR_h, -alkylN(R_e)C(O)OR_f, -alkylN(R_e)$SO_2NR_fR_h$, and -alkylN(R_e)C(O)NR_fR_h;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -S(O)R_f, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -C(O)R_f, -C(O)OR_f and -C(O)NR_fR_h;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)C(O)NH_2, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -C(O)NH_2, -C(O)NH_2, -C(O)N(H)(alkyl), and -C(O)$N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl, cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with

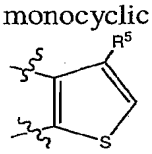
0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(alkyl), -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, $-alkylNH_2$, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), $-alkylSO_2alkyl$, $-alkylN(alkyl)_2$, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bNalkyl$-, $R_aOalkyl$-, $R_aR_bNC(O)$-, $R_aR_bNC(O)alkyl$, R_aS-, $R_aS(O)$-, R_aSO_2-, $R_aSalkyl$-, $R_a(O)Salkyl$-, R_aSO_2alkyl-, $R_aOC(O)$-, $R_aOC(O)alkyl$-, $R_aC(O)$-, $R_aC(O)alkyl$-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, $-(alkyl)(OR_c)$, $-(alkyl)(NR_cR_d)$, $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

m is 0, 1, 2, 3, or 4; and

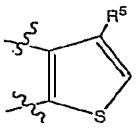
n is 0, 1, 2, 3, or 4;

with the proviso that when A is a monocyclic ring other than



and R^4 is alkoxy, aryloxy, hydroxy or R_eS-, and R^5 is hydrogen, alkenyl, alkoxy, alkyl, alkynyl, aryl, halo, heteroaryl, heterocyclealkyl, cycloalkyl, cyano, nitro, R_aR_bN-, $R_aC(O)$-, R_aS-, $R_a(O)S$-, $R_a(O)_2S$-, $R_aSO_2N(R_f)$-, $R_aR_bNC(O)$-, $R_kOC(O)$-, $R_aR_bNSO_2$- or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl;

and with the further proviso that when A is

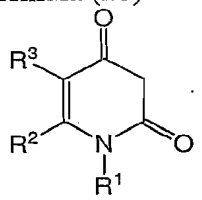


and R^4 is hydroxy or R_eS-, and R^5 is hydrogen, unsubstituted alkyl, halo or $-OR_k$, and R^6 is hydrogen, alkyl, alkenyl, alkynyl, halo, cyano, nitro, aryl, heteroaryl, heterocyclealkyl, $-SR_a$, $-S(O)R_a$, $-S(O)_2R_a$, $-OR_k$, $-N(R_a)(R_b)$, $-C(O)R_a$, $-C(O)OR_a$ and $-C(O)NR_aR_b$, then R^1 is not hydrogen, alkenyl, alkyl, alkynyl, aryl, arylalkenyl, arylalkyl, cycloalkyl, (cycloalkyl)alkenyl,

(cycloalkyl)alkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocyclealkenyl or heterocyclealkyl;

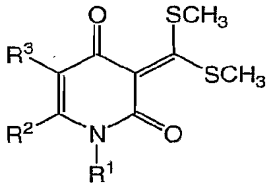
comprising:

(a) contacting a compound of formula (26)



(26)

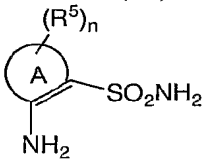
with tris(methylthio)methyl methyl sulfate in the presence of a base to provide a compound of formula (27)



(27);

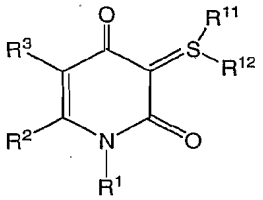
and

(b) contacting the compound of formula (27) with a compound of formula (13)



(13).

In a sixty-first embodiment, the present invention provides a compound having formula (IX)



(IX)

or a pharmaceutically acceptable salt form, tautomer or stereoisomer thereof, wherein

R^1 is selected from the group consisting of hydrogen, alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, (cycloalkyl)alkenyl, (cycloalkyl)alkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl,

hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bNalkyl$-, $R_aR_bNC(O)alkyl$-, $R_aR_bNC(O)Oalkyl$-, $R_aR_bNC(O)NR_calkyl$-, $R_fR_gC=N$- and R_kO-, wherein R^1 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_e), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_e)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_e$;

R^2 and R^3 are independently selected from the group consisting of hydrogen, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonyl, alkyl, aryl, arylalkyl, heteroaryl, heterocycle, heteroarylalkyl, cyano, halo, -$N(R_a)(R_b)$, $R_aR_bNC(O)$-, -SR_a, -$S(O)R_a$, -$S(O)_2R_a$ and $R_aC(O)$-; wherein R^2 and R^3 are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of R_a, alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$;

alternatively, R^2 and R^3, together with the carbon atoms to which they are attached form a five- or six-membered ring selected from the group consisting of aryl, cycloalkyl, heteroaryl and heterocycle, wherein said aryl, cycloalkyl, heteroaryl and heterocycle is optionally substituted with $(R^6)_m$;

R^6 is independently selected at each occurrence from the group consisting of alkyl, alkenyl, alkynyl, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, heterocyclealkyl, -(alkyl)(OR_k), -(alkyl)(NR_aR_b), -SR_a, -$S(O)R_a$, -$S(O)_2R_a$, -OR_k, -$N(R_a)(R_b)$, -$C(O)R_a$, -$C(O)OR_a$ and -$C(O)NR_aR_b$; wherein each R^6 is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, haloalkyl, cyano, nitro, -OR_a, -NR_aR_b, -SR_a, -SOR_a, -SO_2R_a, -$C(O)OR_a$, -$C(O)NR_aR_b$ and -$NC(O)R_a$;

R_a and R_b, at each occurrence, are independently selected from the group consisting of hydrogen, alkenyl, alkyl, alkylsulfanylalkyl, aryl, arylalkenyl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkylcarbonyl, nitroalkyl, R_cR_dN-, R_kO-, $R_kOalkyl$-, $R_cR_dNalkyl$-, $R_cR_dNC(O)alkyl$-, R_cSO_2-, R_cSO_2alkyl-, $R_cC(O)$-, $R_cC(O)alkyl$-, $R_cOC(O)$-, $R_cOC(O)alkyl$-, $R_cR_dNalkylC(O)$-, $R_cR_dNC(O)$-, $R_cR_dNC(O)Oalkyl$-, $R_cR_dNC(O)N(R_e)alkyl$-, wherein R_a and R_b are substituted with 0, 1 or 2 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

alternatively, R_a and R_b, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and

heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), -alkyl$SO_2NR_cR_d$, -alkyl$C(O)NR_cR_d$, -SR_c, -$S(O)R_c$, -$S(O)_2R_c$, -OR_c, -$N(R_c)(R_d)$, -$C(O)R_c$, -$C(O)OR_c$ and -$C(O)NR_cR_d$;

R_c and R_d, at each occurrence, are independently selected from the group consisting of hydrogen, -NR_fR_h, -OR_f, -$CO(R_f)$, -SR_f, -SOR_f, -SO_2R_f, -$C(O)NR_fR_h$, -$SO_2NR_fR_h$, -$C(O)OR_f$, alkenyl, alkyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, aryl, arylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle and heterocyclealkyl; wherein each R_c and R_d is independently substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$, -$C(O)NR_fR_h$, -$C(O)N(H)NR_fR_h$, -$N(R_e)C(O)OR_f$, -$N(R_e)SO_2NR_fR_h$, -$N(R_e)C(O)NR_fR_h$, -alkyl$N(R_e)C(O)OR_f$, -alkyl$N(R_e)SO_2NR_fR_h$, and -alkyl$N(R_e)C(O)NR_fR_h$;

alternatively, R_c and R_d, together with the nitrogen atom to which they are attached form a three- to six-membered ring selected from the group consisting of heteroaryl and heterocycle, wherein the heteroaryl and heterocycle are independently substituted with 0, 1, 2 or 3 substituents independentlyselected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_f), -(alkyl)(NR_fR_h), -SR_f, -$S(O)R_f$, -$S(O)_2R_f$, -OR_f, -$N(R_f)(R_h)$, -$C(O)R_f$, -$C(O)OR_f$ and -$C(O)NR_fR_h$;

R_e is selected from the group consisting of hydrogen, alkenyl, alkyl and cycloalkyl;

R_f, R_g and R_h, at each occurrence, are independently selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkenyl, cycloalkenylalkyl, heterocycle, heterocyclealkyl, heteroaryl and heteroarylalkyl; wherein each R_f, R_g and R_h is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), -NH_2, -N(H)(alkyl), -$N(alkyl)_2$, -S(alkyl), -S(O)(alkyl), -SO_2alkyl, -alkyl-OH, -alkyl-O-alkyl, -alkylNH_2, -alkylN(H)(alkyl), -alkyl$N(alkyl)_2$, -alkylS(alkyl), -alkylS(O)(alkyl), -alkylSO_2alkyl, -N(H)$C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, -$C(O)NH_2$, -$C(O)NH_2$, -C(O)N(H)(alkyl), and -$C(O)N(alkyl)_2$;

alternatively, R_f and R_g together with the carbon atom to which they are attached form a three- to seven-membered ring selected from the group consisting of cycloalkyl,

cycloalkenyl and heterocycle;

alternatively, R_f and R_h together with the nitrogen atom to which they are attached form a three- to seven-membered ring selected from the group consisting of heterocycle and heteroaryl; wherein each of the heterocycle and heteroaryl is independently substituted with 0, 1, 2 or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, cyano, halo, oxo, nitro, aryl, arylalkyl, cycloalkyl, cycloalkenyl, heterocycle, heteroaryl, heteroarylalkyl, –OH, -O(alkyl), $-NH_2$, -N(H)(alkyl), $-N(alkyl)_2$, -S(alkyl), -S(alkyl)$_2$, -S(O)(alkyl), -alkyl-OH, -alkyl-O-alkyl, $-alkylNH_2$, -alkylN(H)(alkyl), -alkylS(alkyl), -alkylS(O)(alkyl), $-alkylSO_2alkyl$, $-alkylN(alkyl)_2$, $-N(H)C(O)NH_2$, -C(O)OH, -C(O)O(alkyl), -C(O)alkyl, $-C(O)NH_2$, $-C(O)NH_2$, -C(O)N(H)(alkyl), and $-C(O)N(alkyl)_2$;

R_k is selected from the group consisting of hydrogen, alkenyl, alkyl, aryl, arylalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, nitroalkyl, $R_aR_bNalkyl$-, $R_aOalkyl$-, $R_aR_bNC(O)$-, $R_aR_bNC(O)alkyl$, R_aS-, $R_aS(O)$-, R_aSO_2-, $R_aSalkyl$-, $R_a(O)Salkyl$-, R_aSO_2alkyl-, $R_aOC(O)$-, $R_aOC(O)alkyl$-, $R_aC(O)$-, $R_aC(O)alkyl$-, wherein each R_k is substituted with 0, 1, 2, or 3 substituents independently selected from the group consisting of alkyl, alkenyl, alkynyl, oxo, halo, cyano, nitro, haloalkyl, haloalkoxy, aryl, heteroaryl, heterocycle, arylalkyl, heteroarylalkyl, alkoxyalkoxyalkyl, -(alkyl)(OR_c), -(alkyl)(NR_cR_d), $-SR_c$, $-S(O)R_c$, $-S(O)_2R_c$, $-OR_c$, $-N(R_c)(R_d)$, $-C(O)R_c$, $-C(O)OR_c$ and $-C(O)NR_cR_d$;

m is 0, 1, 2, 3, or 4; and

R^{11} and R^{12} are independently selected from the group consisting of alkyl, alkenyl and alkynyl.

Exemplary compounds of the sixty-first embodiment of the present invention of formula (IX), or a pharmaceutically acceptable salt form, tautomer or stereoisomer thereof, include, but not limited to, the following:

1-benzyl-3-(bis(methylthio)methylene)-1H-quinoline-2,4(1*H*,3*H*)-dione;

3-[bis(methylthio)methylene]-1-butyl-1,8-naphthyridine-2,4(1*H*,3*H*)-dione;

3-[bis(methylthio)methylene]-1-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)quinoline-2,4(1*H*,3*H*)-dione;

3-[bis(methylthio)methylene]-1-[(cyclopropylmethyl)amino]quinoline-2,4(1*H*,3*H*)-dione;

3-[bis(methylthio)methylene]-1-(3-methylbutyl)pyridine-2,4(1*H*,3*H*)-dione;

1-benzyl-3-[bis(methylthio)methylene]pyridine-2,4(1*H*,3*H*)-dione;

3-[bis(methylthio)methylene]-1-(cyclobutylamino)quinoline-2,4(1*H*,3*H*)-dione; and

3-[bis(methylthio)methylene]-1-(cyclobutylmethyl)pyridine-2,4(1*H*,3*H*)- dione.

The compounds of the invention can comprise asymmetrically substituted carbon

atoms. As a result, all stereoisomers of the compounds of the invention are meant to be included in the invention, including racemic mixtures, mixtures of diastereomers, mixtures of enantiomers, as well as individual optical isomers, including, enantiomers and single diastereomers of the compounds of the invention substantially free from their enantiomers or other diastereomers. By "substantially free" is meant greater than about 80% free of other enantiomers or diastereomers of the compound, more preferably greater than about 90% free of other enantiomers or diastereomers of the compound, even more preferably greater than about 95% free of other enantiomers or diastereomers of the compound, even more highly preferably greater than about 98% free of other enantiomers or diastereomers of the compound and most preferably greater than about 99% free of other enantiomers or diastereomers of the compound.

In addition, compounds comprising the possible geometric isomers of carbon-carbon double bonds and carbon-nitrogen double are also meant to be included in this invention.

Individual stereoisomers of the compounds of this invention can be prepared by any one of a number of methods which are within the knowledge of one of ordinary skill in the art. These methods include stereospecific synthesis, chromatographic separation of diastereomers, chromatographic resolution of enantiomers, conversion of enantiomers in an enantiomeric mixture to diastereomers and then chromatographically separating the diastereomers and regeneration of the individual enantiomers, enzymatic resolution and the like.

Stereospecific synthesis involves the use of appropriate chiral starting materials and synthetic reactions which do not cause racemization or inversion of stereochemistry at the chiral centers.

Diastereomeric mixtures of compounds resulting from a synthetic reaction can often be separated by chromatographic techniques which are well-known to those of ordinary skill in the art.

Chromatographic resolution of enantiomers can be accomplished on chiral chromatography resins. Chromatography columns containing chiral resins are commercially available. In practice, the racemate is placed in solution and loaded onto the column containing the chiral stationary phase. The enantiomers are then separated by HPLC.

Resolution of enantiomers can also be accomplished by converting the enantiomers in the mixture to diastereomers by reaction with chiral auxiliaries. The resulting diastereomers can then be separated by column chromatography. This technique is especially useful when the compounds to be separated contain a carboxyl, amino or hydroxyl group that will form a salt or covalent bond with the chiral auxiliary. Chirally pure amino acids, organic carboxylic acids or organosulfonic acids are especially useful as chiral auxiliaries. Once the diastereomers have been separated by chromatography, the individual enantiomers can be

regenerated. Frequently, the chiral auxiliary can be recovered and used again.

Enzymes, such as esterases, phosphatases and lipases, can be useful for resolution of derivatives of the enantiomers in an enantiomeric mixture. For example, an ester derivative of a carboxyl group in the compounds to be separated can be prepared. Certain enzymes will selectively hydrolyze only one of the enantiomers in the mixture. Then the resulting enantiomerically pure acid can be separated from the unhydrolyzed ester.

The present compounds may exhibit the phenomena of tautomerism or structural isomerism. As the drawings within this specification can only represent one possible tautomeric or structural isomeric form, it should be understood that the invention encompasses any tautomeric or structural isomeric form; or mixtures thereof, which possess the ability to inhibit hepatitis C, and is not limited to any one tautomeric or structural isomeric form utilized within the drawings.

In addition, solvates and hydrates of the compounds of the invention are meant to be included in this invention.

When any variable (for example R^1, R^2, R^3, m, n, etc.) occurs more than one time in any substituent or in the compound of the invention or any other formula herein, its definition on each occurrence is independent of its definition at every other occurrence. In addition, combinations of substituents are permissible only if such combinations result in stable compounds. Stable compounds are compounds which can be isolated in a useful degree of purity from a reaction mixture.

The compounds of the present invention can exist as pharmaceutically acceptable salts. The term "pharmaceutically acceptable salt," as used herein, represents acid or base salts or zwitterionic forms of the compounds of the present invention which are water or oil-soluble or dispersible, which are suitable for treatment of diseases without undue toxicity, irritation, and allergic response; which are commensurate with a reasonable benefit/risk ratio, and which are effective for their intended use. The salts can be prepared during the final isolation and purification of the compounds or separately by reacting a basic group (for example, a nitrogen containing group) with a suitable acid. Representative acid addition salts include acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, glycerophosphate, hemisulfate, heptanoate, hexanoate, formate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethansulfonate, lactate, maleate, mesitylenesulfonate, methanesulfonate, naphthylenesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, pamoate, pectinate, persulfate, 3-phenylproprionate, picrate, pivalate, propionate, succinate, tartrate, trichloroacetate,trifluoroacetate, phosphate, glutamate, bicarbonate, para-toluenesulfonate, and undecanoate. Also, amino groups in the compounds of the present invention can be quaternized with methyl, ethyl, propyl, and butyl chlorides, bromides, and iodides; dimethyl,

diethyl, dibutyl, and diamyl sulfates; decyl, lauryl, myristyl, and steryl chlorides, bromides, and iodides; and benzyl and phenethyl bromides. Examples of acids which can be employed to form pharmaceutically acceptable addition salts include inorganic acids such as hydrochloric, hydrobromic, sulfuric, and phosphoric, and organic acids such as oxalic, maleic, succinic, and citric.

Basic addition salts can be prepared during the final isolation and purification of the compounds by reacting an acidic group (for example, a carboxy group or an enol) with a suitable base such as the hydroxide, carbonate, or bicarbonate of a metal cation or with ammonia or an organic primary, secondary, or tertiary amine. The cations of pharmaceutically acceptable salts include lithium, sodium, potassium, calcium, magnesium, and aluminum, as well as nontoxic quaternary amine cations such as ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, diethylamine, ethylamine, tributylamine, pyridine, N,N-dimethylaniline, N-methylpiperidine, N-methylmorpholine, dicyclohexylamine, procaine, dibenzylamine, N,N-dibenzylphenethylamine, 1-ephenamine, and N,N'-dibenzylethylenediamine. Other representative organic amines useful for the formation of basic addition salts include ethylenediamine, ethanolamine, diethanolamine, piperidine, and piperazine.

Preferred salts of the compounds of the present invention include monosodium, disodium, triethylamine salt, trifluoroacetate and hydrochloride.

The present compounds can also exist as pharmaceutically acceptable prodrugs. The term "pharmaceutically acceptable prodrug," refers to those prodrugs or zwitterions which are suitable for use in contact with the tissues of patients without undue toxicity, irritation, and allergic response, are commensurate with a reasonable benefit/risk ratio, and are effective for their intended use. "Prodrugs" are considered to be any covalently bonded carriers which release the active parent drug of formula (I), (II), (III), (IV), (V), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) in vivo when such prodrugs is administered to a mammalian subject. Prodrugs of the compounds of formula (I), (II), (III), (IV), (V), (Va), (Vb), (VIa), (VIb), (VII) or (VIII) are prepared by modifying functional groups present in the compounds in such a way that the modifications are cleaved, either in routine manipulation or in vivo, to the parent compounds respectively. Prodrugs include compounds wherein hydroxy, amine, carboxy, or sulfhydryl groups are bonded to any group that, when administered to a mammalian subject, cleaves to form a free hydroxyl, amino, carboxy, or sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate, and benzoate derivatives of the hydroxy, carboxy and amine functional groups in the compounds of formula (I), (II), (III), (IV), (V), (Va), (Vb), (VIa), (VIb), (VII) and (VIII); and the like.

In accordance with methods of treatment and pharmaceutical compositions of the invention, the compounds can be administered alone or in combination with other antiviral

agents. When using the compounds, the specific pharmaceutically effective dose level for any particular patient will depend upon factors such as the disorder being treated and the severity of the disorder; the activity of the particular compound used; the specific composition employed; the age, body weight, general health, sex, and diet of the patient; the time of administration; the route of administration; the rate of excretion of the compound employed; the duration of treatment; and drugs used in combination with or coincidently with the compound used. The compounds can be administered orally, parenterally, osmotically (nasal sprays), rectally, vaginally, or topically in unit dosage formulations containing carriers, adjuvants, diluents, vehicles, or combinations thereof. The term "parenteral" includes infusion as well as subcutaneous, intravenous, intramuscular, and intrasternal injection.

Parenterally administered aqueous or oleaginous suspensions of the compounds can be formulated with dispersing, wetting, or suspending agents. The injectable preparation can also be an injectable solution or suspension in a diluent or solvent. Among the acceptable diluents or solvents employed are water, saline, Ringer's solution, buffers, monoglycerides, diglycerides, fatty acids such as oleic acid, and fixed oils such as monoglycerides or diglycerides.

The antiviral effect of parenterally administered compounds can be prolonged by slowing their absorption. One way to slow the absorption of a particular compound is administering injectable depot forms comprising suspensions of crystalline, amorphous, or otherwise water-insoluble forms of the compound. The rate of absorption of the compound is dependent on its rate of dissolution which is, in turn, dependent on its physical state. Another way to slow absorption of a particular compound is administering injectable depot forms comprising the compound as an oleaginous solution or suspension. Yet another way to slow absorption of a particular compound is administering injectable depot forms comprising microcapsule matrices of the compound trapped within liposomes, microemulsions, or biodegradable polymers such as polylactide-polyglycolide, polyorthoesters or polyanhydrides. Depending on the ratio of drug to polymer and the composition of the polymer, the rate of drug release can be controlled.

Transdermal patches can also provide controlled delivery of the compounds. The rate of absorption can be slowed by using rate controlling membranes or by trapping the compound within a polymer matrix or gel. Conversely, absorption enhancers can be used to increase absorption.

Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In these solid dosage forms, the active compound can optionally comprise diluents such as sucrose, lactose, starch, talc, silicic acid, aluminum hydroxide, calcium silicates, polyamide powder, tableting lubricants, and tableting aids such as magnesium stearate or microcrystalline cellulose. Capsules, tablets and pills can also comprise buffering

agents, and tablets and pills can be prepared with enteric coatings or other release-controlling coatings. Powders and sprays can also contain excipients such as talc, silicic acid, aluminum hydroxide, calcium silicate, polyamide powder, or mixtures thereof. Sprays can additionally contain customary propellants such as chlorofluorohydrocarbons or substitutes therefore.

Liquid dosage forms for oral administration include emulsions, microemulsions, solutions, suspensions, syrups, and elixirs comprising inert diluents such as water. These compositions can also comprise adjuvants such as wetting, emulsifying, suspending, sweetening, flavoring, and perfuming agents.

Topical dosage forms include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants, and transdermal patches. The compound is mixed under sterile conditions with a carrier and any needed preservatives or buffers. These dosage forms can also include excipients such as animal and vegetable fats, oils, waxes, paraffins, starch, tragacanth, cellulose derivatives, polyethylene glycols, silicones, bentonites, silicic acid, talc and zinc oxide, or mixtures thereof. Suppositories for rectal or vaginal administration can be prepared by mixing the compounds with a suitable non-irritating excipient such as cocoa butter or polyethylene glycol, each of which is solid at ordinary temperature but fluid in the rectum or vagina. Ophthalmic formulations comprising eye drops, eye ointments, powders, and solutions are also contemplated as being within the scope of this invention.

The compounds of the invention inhibit HCV RNA dependent RNA polymerase an enzyme essential for HCV viral replication. They can be administered as the sole active pharmaceutical agent, or they can also be used in combination with one or more agents to treat hepatitis C infections or the symptoms associated with HCV infection. Other agents to be administered in combination with a compound of the present invention include therapies for disease caused by HCV infection that suppresses HCV viral replication by direct or indirect mechanisms. These include agents such as host immune modulators, for example, interferon-alpha, pegylated interferon-alpha, CpG oligonucleotides and the like, or antiviral compounds that inhibit host cellular functions such as inosine monophosphate dehydrogenase, for example, ribavirin and the like. Also included are cytokines that modulate immune function. Also included are vaccines comprising HCV antigens or antigen adjuvant combinations directed against HCV. Also included are agents that interact with host cellular components to block viral protein synthesis by inhibiting the internal ribosome entry site (IRES) initiated translation step of HCV viral replication or to block viral particle maturation and release with agents targeted toward the viroporin family of membrane proteins such as, for example, HCV P7 and the like. Other agents to be administered in combination with a compound of the present invention include any agent or combination of agents that inhibit the replication of HCV by targeting proteins of the viral genome involved in the viral replication. These agents include but are not limited to other inhibitors of HCV

RNA dependent RNA polymerase such as, for example, nucleoside type polymerase inhibitors described in WO0190121(A2), or US6348587B1 or WO0160315 or WO0132153 or non-nucleoside inhibitors such as, for example, benzimidazole polymerase inhibitors described in EP1162196A1 or WO0204425 or inhibitors of HCV protease such as, for example, peptidomimetic type inhibitors such as BILN2061 and the like or inhibitors of HCV helicase.

Other agents to be administered in combination with a compound of the present invention include any agent or combination of agents that inhibit the replication of other viruses for co-infected individuals. These agent include but are not limited to therapies for disease caused by hepatitis B (HBV) infection such as, for example, adefovir, lamivudine, LdT (L-deoxythymidine) and tenofovir or therapies for disease caused by human immunodeficiency virus (HIV) infection such as, for example, protease inhibitors: ritonavir, lopinavir, indinavir, nelfinavir, saquinavir, amprenavir, atazanavir, tipranavir, TMC-114, fosamprenavir; reverse transcriptase inhibitors: zidovudine, lamivudine, didanosine, stavudine, tenofovir, zalcitabine, abacavir, efavirenz, nevirapine, delavirdine, TMC-125; integrase inhibitors: L-870812, S-1360, or entry inhibitors: enfuvirtide (T-20), T-1249.

Other agents to be administered in combination with a compound of the present invention include any agent or combination of agents that treat or alleviate symptoms of HCV infection including cirrhosis and inflammation of the liver.

When administered as a combination, the therapeutic agents can be formulated as separate compositions which are given at the same time or within a predetermined period of time, or the therapeutic agents can be given as a single unit dosage form.

The total daily dose of the compounds administered to a host in single or divided doses can be in amounts from about 0.1 to about 200 mg/kg body weight or preferably from about 0.25 to about 100 mg/kg body weight. Single dose compositions can contain these amounts or submultiples thereof to make up the daily dose.

Determination of Biological Activity

HCV polymerase inhibition assay: biochemical IC_{50}:

Either two-fold serial dilutions (fractional inhibition assay) or a narrower range of dilutions spanning the IC50 of the inhibitor (tight binding assay) of the inhibitors were incubated with 20 mM Tris-Cl pH 7.5, 5 mM $MgCl_2$, 50 mM NaCl, 1 mM dithiothreitol, 1 mM ethylene diamine tetraacetic acid (EDTA), 300 μM GTP and 150 to 300 nM NS5B (HCV Strain 1B (J4, Genbank accession number AF054247, or H77, Genbank accession number AF011751)) for 15 minutes at room temperature. The reaction was initiated by the addition of 20 μM CTP, 20 μM ATP, 1 μM 3H-UTP (10 mCi/umol), 150 nM template RNA and 0.4 U/μl RNase inhibitor (RNasin, Promega), and allowed to proceed for 2 to 4 hours at room temperature. Reaction volume was 50 μl. The reaction was terminated by the addition

of 1 volume of 4 mM spermine in 10 mM Tris-Cl pH 8.0, 1 mM EDTA. After incubation for at least 15 minutes at room temperature, the precipitated RNA was captured by filtering through a GF/B filter (Millipore) in a 96 well format. The filter plate was washed three times with 200 µl each of 2 mM spermine, 10 mM Tris-Cl pH 8.0, 1 mM EDTA, and 2 times with ethanol. After air drying, 30 µl of Microscint 20 scintillation cocktail (Packard) was added to each well, and the retained cpm were determined by scintillation counting. IC50 values were calculated by a two-variable nonlinear regression equation using an uninhibited control and a fully inhibited control sample to determine the minimum and maximum for the curve. Tight-binding assays were performed on those compounds exhibiting IC50 values less than 0.15 µM in the fractional inhibition assay in order to more precisely measure the IC50 values. Retained cpm were plotted vs. inhibitor concentration and fit to equation 1 using non-linear regression (ref. 1) to obtain the IC50 values.

Retained cpm = $A[sqrt\{(IC_{50} + I_t - E_t)^2 + 4IC_{50}E_t\} - (IC_{50} + I_t - E_t)]$ eqn 1.

where $A = V_{max}[S]/2(K_m + [S])$; I_t = total inhibitor concentration and E_t= total active concentration of enzyme.

Ref. 1: Morrison, J. F. and S. R. Stone. 1985. Approaches to the study and analysis of the inhibition of enzymes by slow- and tight-binding inhibitors. Comments Mol. Cell. Biophys. **2:** 347-368.

The sequence of the template RNA used was:

5'GGGCGAAUUGGGCCCUCUAGAUGCAUGCUCGAGCGGCCGCCAGUGUGAUGG AUAUCUGCAGAAUUCGCCCUUGGUGGCUCCAUCUUAGCCCUAGUCACGGCUAG CUGUGAAAGGUCCGUGAGCCGCUUGACUGCAGAGAGUGCUGAUACUGGCCUCU CUGCAGAUCAAGUC-3'

When tested by the above method, the compounds of the present invention inhibit HCV polymerase 1B with IC50's in the range of 0.002 µM to 500 µM.

Evaluation of the HCV inhibitors in HCV replicon: cell culture EC_{50}

The cell lines and assays were conducted according to the methods described by Ikeda M, Yi M, Li K, Lemon SM., J Virol 2002 Mar;76(6):2997-3006, and Blight K. J, Kolykhalov A., Rice C. M., Science 2000 Dec, 290:1972-1974) with the following modifications:

RNA assay

Replicon cells were plated at $3x10^3$ cells per well in 96-well plate in DMEM medium containing 5% fetal calf serum. At day 1, culture medium was removed and replaced with fresh medium containing eight serial 2-fold dilutions of compound. The final concentration of DMSO in medium was 0.5%. The untreated control culture was treated in an identical manner except no inhibitor was added to the medium. Plates were incubated in a CO_2 incubator at 37°C. On Day 4, 100 µl lysis buffer (RTL) (Qiagen) was added to each well

after removal of culture medium. RNA was purified according to manufacturer's recommendations (Qiagen RNAeasy) and eluted in 200 μl of water. The HCV RNA level was quantified from a portion (5 μl out of 200 μl) of the purified RNA by real-time RT-PCR method. The primers and probe are derived from specific sequence in the 5'UTR region. RT-PCR reaction was performed at 48°C for 30 min, followed by 40 cycles set to 95°C, 15 s; 54°C, 30 s; and 72°C, 40 s. The percentage reduction of HCV RNA in the presence of compound was calculated and the 50% inhibitory concentration (IC_{50}) was calculated by non-linear regression analysis using the Prism program.

When tested by the above method, the compounds of the present invention inhibit replicon production with EC50's in the range of 0.002 μM to >100 μM.

Cytotoxity assays

Cytotoxicity assays were performed in replicon cells. Briefly, HCV replicon cells were plated at $3x10^3$ cells per well in 96-well plate in DMEM medium containing 5% FCS. At day 1, culture medium was removed and replaced with fresh medium containing eight serial 2-fold dilutions of compound. The final concentration of DMSO in medium was 0.5%. All experiments were performed in duplicate. The untreated control culture was treated in an identical manner except no inhibitor was added to the medium. Plates were incubated in a CO_2 incubator at 37°C. On day 4, stock solution of the tetrazolium salt, MTT (4 mg/ml in PBS, Sigma cat.# M 2128) was added to each well at 25 μl per well. Plates were further incubated for 4 hours, treated with 20% SDS plus 0.02 N HCl at 50 μl per well to lyse the cells. After an overnight incubation, optical density was measured by reading the plates at 570/650 nm wavelengths. The percent reduction of formazan blue color formed relative to control was calculated and the cytopathic effect was described as a 50% toxicity concentration (TC_{50}) was calculated by non-linear regression analysis using the Prism program.

When tested by the above method, the compounds of the present invention exhibited CPE reduction with TC50's in the range of 6.6 μM to >100 μM.

Cell culture assays for agents targeted toward hepatitis C are not yet available because of the inability to produce infectious virus in a sustained cell line. The hepatitis C virus genome encodes a large polyprotein, which after processing produces the necessary functional components to synthesize progeny RNA. Selectable cell lines that produce high and sustained levels of subgenomic HCV RNA (replicons) have been derived from human hepatoma cells (Huh7) as described in the references above. The mechanism of RNA replication in these cell lines is considered to be identical to the replication of full length HCV RNA in infected hepatocytes. The compounds and methods of this invention are inhibitors of HCV RNA replication in the replicon assay systems described above. This forms the basis of the claim for their potential as therapies in treating disease resulting from

hepatitis C viral infection.

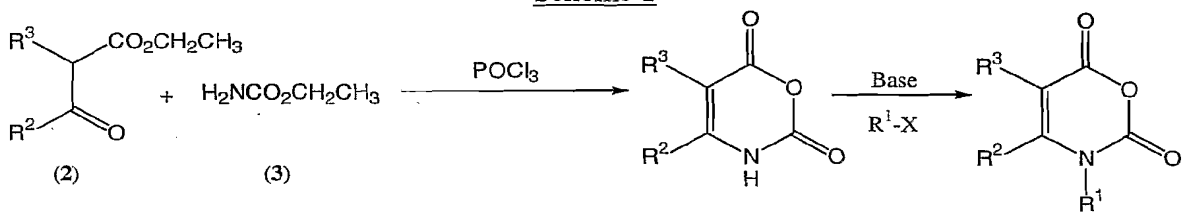
Synthetic Methods

Abbreviations which have been used in the descriptions of the scheme and the examples that follow are: DMF is N,N-dimethylformamide, DMSO is dimethylsulfoxide, and THF is tetrahydrofuran.

The compounds and processes of the present invention will be better understood in connection with the following synthetic schemes which illustrate the methods by which the compounds of the invention may be prepared. Starting materials can be obtained from commercial sources or prepared by well-established literature methods known to those of ordinary skill in the art. The groups A, R^1, R^2, R^3, R^4, R^5, and n are as defined above unless otherwise noted below.

This invention is intended to encompass compounds having formula (I) when prepared by synthetic processes or by metabolic processes. Preparation of the compounds of the invention by metabolic processes include those occurring in the human or animal body (*in vivo*) or processes occurring *in vitro*.

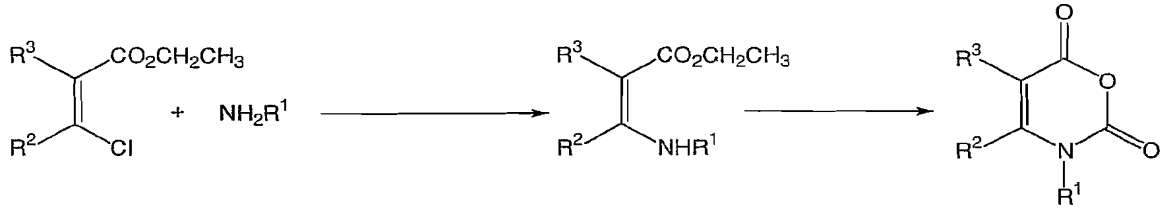
Scheme 1



(2) (3) (4) (5)

As shown in Scheme 1, compounds of formula (2) can be reacted with compounds of formula (3) in the presence of phosphorous oxychloride under heating conditions to provide compounds of formula (4). Compounds of formula (4) can be reacted with a base such as sodium hydride, potassium hydride, lithium hexamethyldisilazide, and the like in solvent such as but not limited to dimethylacetamide, dimethylformamide, THF, and the like, followed by the addition of R^1-X, (wherein R^1 is alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, haloalkoxyalkyl, haloalkyl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl- or $R_aR_bNC(O)NR_c$alkyl-, and wherein X is Br, Cl, I, $CF_3S(O)_2$-, $CH_3S(O)_2$-, or tosyl) to provide compounds of formula (5).

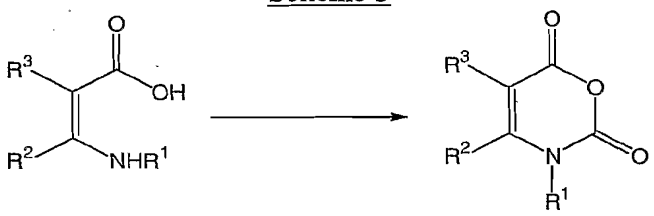
Scheme 2



(6) (7) (8) (5)

Alternatively, compounds of formula (**6**) can be treated with compounds of formula (**7**) (wherein R^1 is alkenyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, alkynyl, aryl, arylalkenyl, arylalkyl, arylsulfanylalkyl, arylsulfonylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkenyl, cycloalkylalkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkenyl, heteroarylalkyl, heteroarylsulfonylalkyl, heterocycle, heterocyclealkenyl, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_aR_bN-, $R_aR_bN$alkyl-, $R_aR_bNC(O)$alkyl-, $R_aR_bNC(O)O$alkyl-, $R_aR_bNC(O)NR_c$alkyl-, R_fR_gC=N- or R_kO-), under heating conditions optionally in the presence of a base such as potassium carbonate and a catalyst such as copper bromide, to provide compounds of formula (**8**). Compounds of formula (**8**) can be treated with reagents including but not limited to phosgene, diphosgene, triphosgene in solvents such as but not limited to 1,2-dichloroethane, carbon tetrachloride, 1,4-dioxane or mixtures thereof, under heating conditions to provide compounds of formula (**5**).

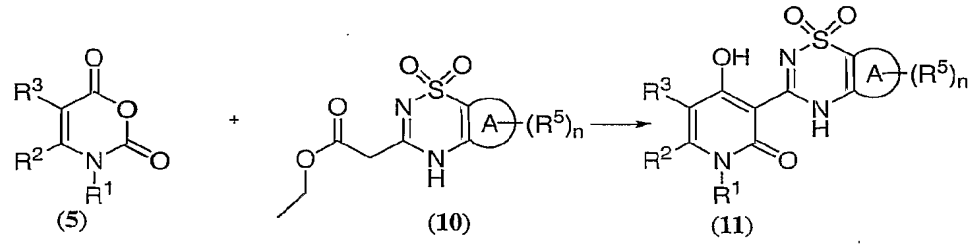
Scheme 3



(9) (5)

In addition, compounds of formula (**9**) can also be reacted with reagents including but not limited to phosgene, diphosgene, triphosgene, carbonyldiimidazole, ethyl chloroformate and the like in the presence of a base such as potassium hydroxide, pyridine, lithium hydroxide, and the like in solvents such as but not limited to water, toluene, benzene, and the like under heating conditions to provide compounds of formula (**5**).

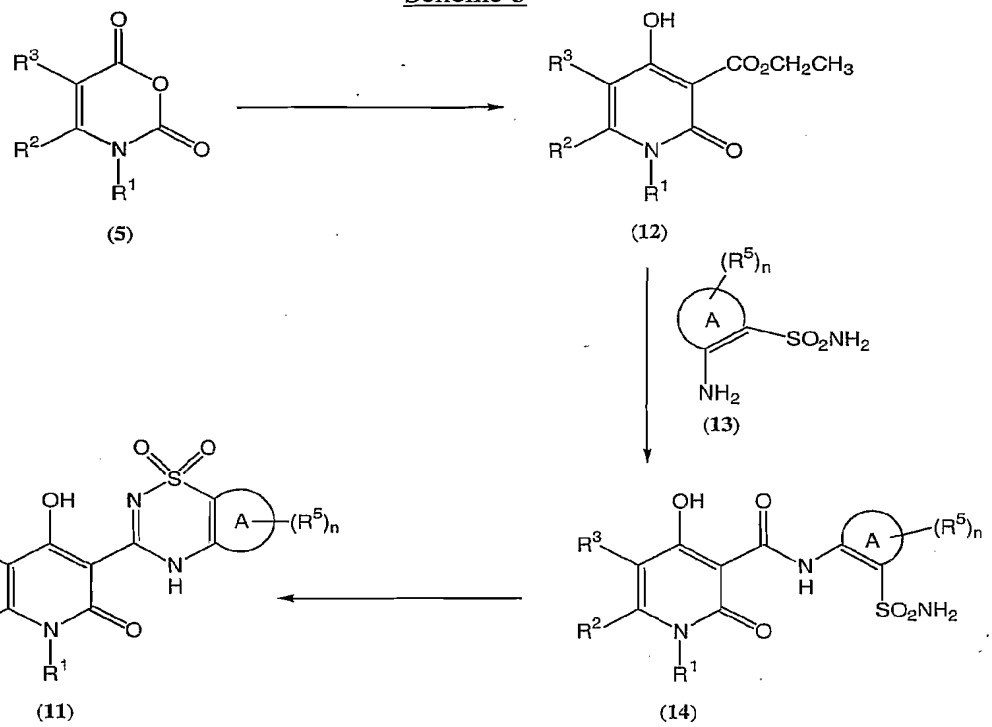
Scheme 4



(5) (10) (11)

Compounds of formula (**5**) can be treated with compounds of formula (**10**) in the presence of a base such as sodium hydride, potassium hydride, lithium hexamethyldisilazide, and the like in a solvent such as but not limited to THF, diethyl ether, methyl tert-butyl ether followed by the treatment with an acid such as acetic acid, dichloroacetic acid or sulfuric acid to provide compounds of formula (**11**) which are representative of a compound of formula (I), where R^4 is hydroxy.

Scheme 5

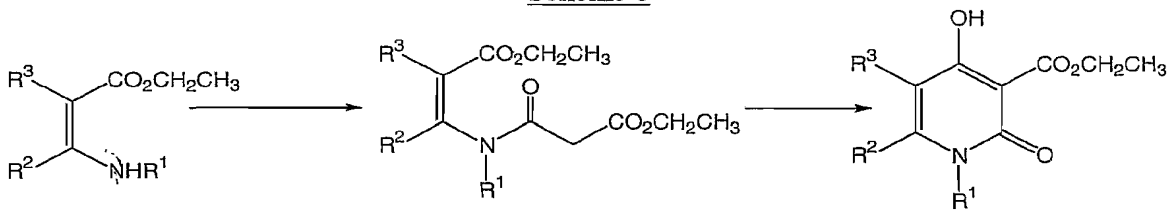


(5) (12) (13) (11) (14)

Compounds of formula (**5**) can be reacted with diethyl malonate that has been pretreated with a base such as sodium hydride, potassium hydride, and the like in solvents such as dimethylacetamide, dimethylformamide, THF, and the like under heated conditions to provide compounds of formula (**12**). Compounds of formula (**12**) can be treated with compounds of formula (**13**) in solvents such as toluene, mesitylene, benzene, and the like under heated conditions to provides compounds of formula (**14**). Compounds of formula (**14**) can be treated with a base such as sodium hydroxide, potassium hydroxide, lithium

hydroxide, and the like in water under heated conditions to provide compounds of formula (**11**).

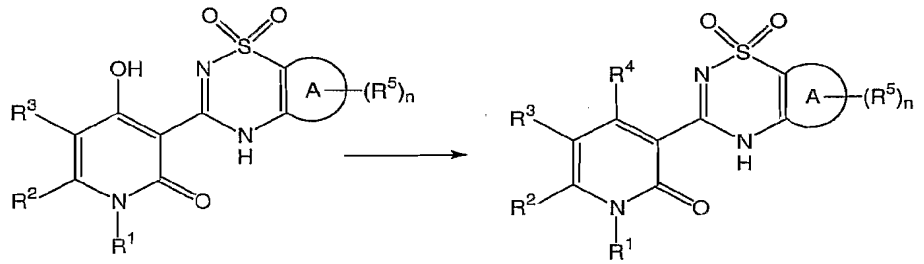
Scheme 6



(**8**) (**15**) (**12**)

Alternatively, compounds of formula (**8**) can be treated with ethyl chloromalonate in the presence of a base such as triethylamine, diisopropylethylamine, pyridine, and the like in solvents such as dichloromethane, chloroform, carbon tetrachloride to provide compounds of formula (**15**). Alternatively, compounds of the formula (**8**) can be treated with ethyl chloromalonate in solvents such as benzene, toluene under heating conditions to provide compounds of formula (**15**). Compounds of formula (**15**) can be treated with sodium ethoxide in ethanol to provide compounds of formula (**12**).

Scheme 7

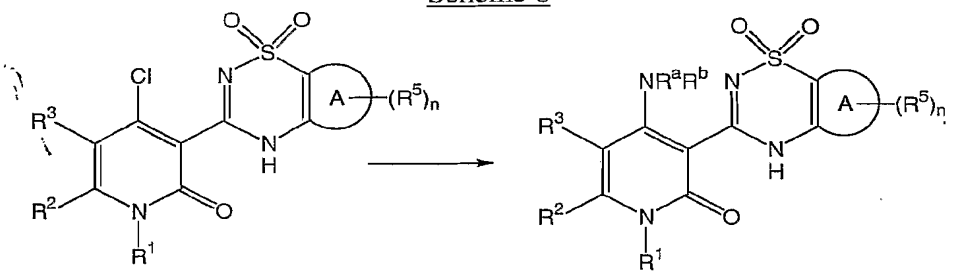


(**11**) (**I**)

Scheme 7 shows the preparation of compounds of formula (**I**)) where R^4 is halo. Compounds of formula (**11**) can be treated with reagents known to those skilled in the art which are commonly used to convert alcohols to chlorides. For example, compounds of formula (**11**) can be treated with reagents including but not limited to PCl_5, PCl_3, $POCl_3$, or thionyl chloride, with or without solvents such as but not limited to dichloromethane, chloroform and benzene, to provide compounds of formula (**I**) which are representative of compounds where R^4 is chlorine. Similar transformations are possible using PBr_3 or DAST to convert the said alcohol to the corresponding compound of formula (**I**) where R^4 is bromide and fluoride, respectively. Alternatively, compound of formula (**I**) wherein R^4 is iodo can be prepared by (a). reacting compound of formula (**11**) with a mesylating reagent

such as methanesulfonyl chloride or methanesulfonyl anhydride in the presence of an amine base such as triethylamine, pyridine or diisopropylethylamine in solvents such as but not limited to dichloromethane, acetonitrile, carbon tetrachloride, chloroform, and (b) treatment of the mesylate thus formed with N-iodosuccinimide.

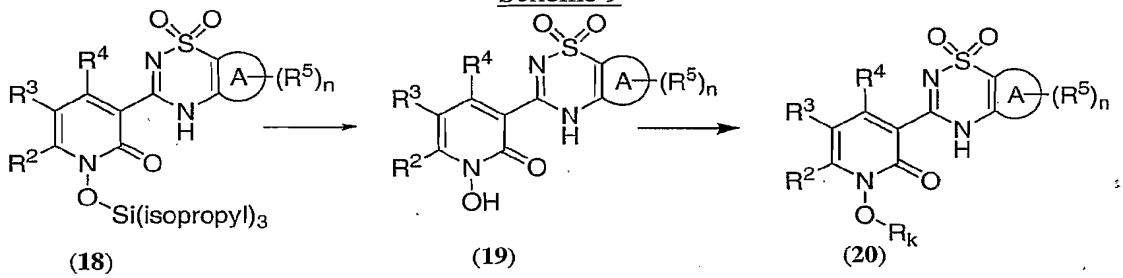
Scheme 8



(16) (17)

As shown in Scheme 8, compounds of formula (**16**) can be converted to compounds of formula (**17**) which are representative of compounds of formula (I) where R^4 is R_aR_bN-, by treatment with an amine having the formula R_aR_bNH, (where R_a and R_b are as defined herein) in a polar solvent such as methanol, ethanol, and the like, under heating conditions to provide compounds of formula (**17**).

Scheme 9

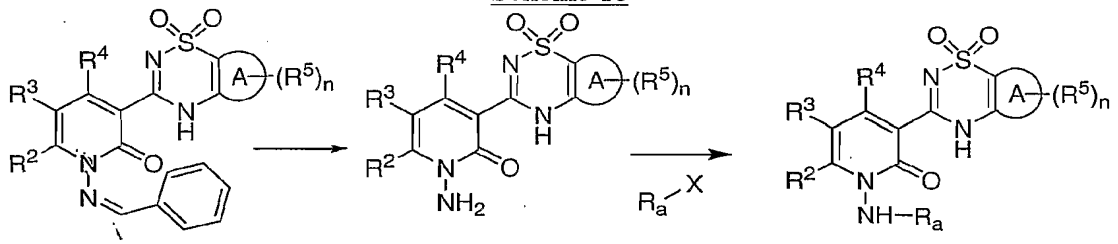


(18) (19) (20)

Compounds of formula (**18**) (which are representative of compounds of formula (I) where R^1 is O-Si(isopropyl)$_3$ or some other easily removed ether protecting group) can be treated with a fluoride containing reagent to provide compounds of formula (**19**). The hydroxyl amine portion of compounds of formula (**19**) can be treated with a base such as sodium hydride in solvents such as dimethylformamide, or lithium hexamethyldisilazide in solvents such as but not limited to THF, dioxane and the like, followed by the addition of R_k-X (wherein R_k is alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonylalkyl, alkylsulfanylalkyl, alkylsulfonylalkyl, aryl, arylalkyl, arylsulfanylalkyl, carboxyalkyl, cyanoalkyl, cycloalkenyl, cycloalkenylalkyl, cycloalkyl, cycloalkylalkyl, formylalkyl, haloalkoxyalkyl, haloalkyl, heteroaryl, heteroarylalkyl, heterocycle, heterocyclealkyl, hydroxyalkyl, nitroalkyl, R_cR_dNalkyl- or R_cR_dNC(O)alkyl, and wherein X

is Br, Cl, I, $CF_3S(O)_2$-, $CH_3S(O)_2$-, or tosyl) to provide compounds of formula (**20**) which are representative of compounds of formula (**I**) where R^1 is defined as R_kO-.

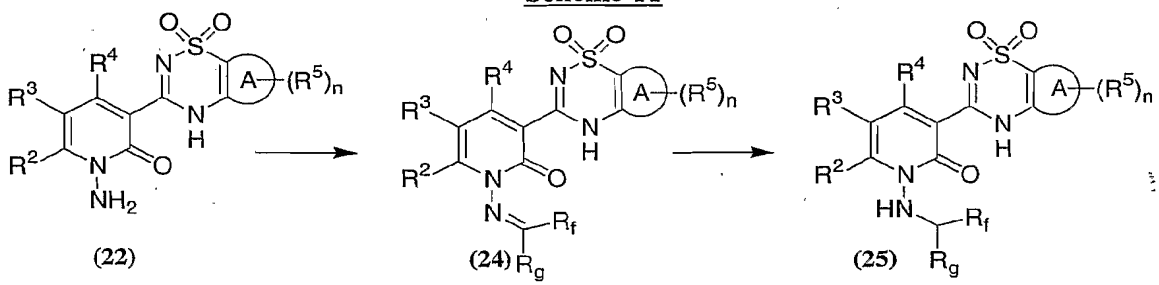
Scheme 10



(21) (22) (23)

Compounds of formula (**21**) can be treated with aqueous base such as but not limited to potassium hydroxide, sodium hydroxide and the like, to provide compounds of formula (**22**). Compounds of formula (**22**) can be treated with a metal hydride base such as sodium hydride, an organolithium reagent (e.g. t-BuLi, n-BuLi, or s-BuLi), or lithium hexamethyldisilazide in an appropriate solvent or a mixture of solvents selected from THF, DMSO, DMF, dioxane, ether, dichloromethane, and the like, followed by the addition of R_aX wherein X is Br, Cl, I, $CF_3S(O)_2$-, $CH_3S(O)_2$-, or tosyl to provide compounds of formula (**23**) which are representative of compounds of formula (I) wherein R^1 is -NHRa.

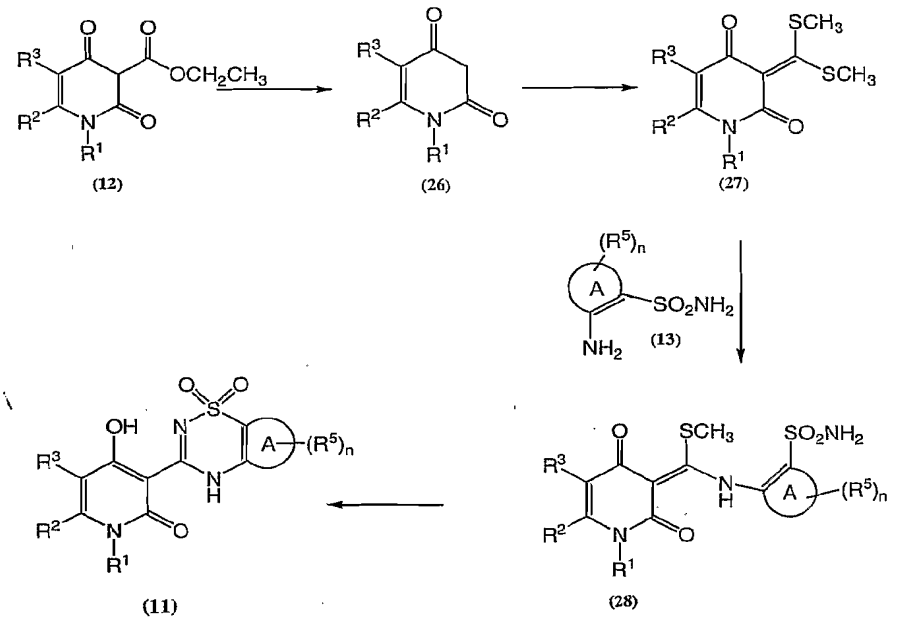
Scheme 11



(22) (24) (25)

Alternatively, compounds of formula (**22**) can be treated with aldehydes or ketones of structure $R_fR_gC(O)$ without solvents or with solvents such as but not limited to dimethylacetamide, tetrahydrofuran, dioxane and the like under heated conditions to provide compounds of formula (**24**). Reduction of compounds of formula (**24**) with hydrogen and a catalyst such as palladium and the like or a metal hydrides such as lithium borohydride, sodium cyanoborohydride and the like provide compounds of the formula (**25**).

Scheme 12

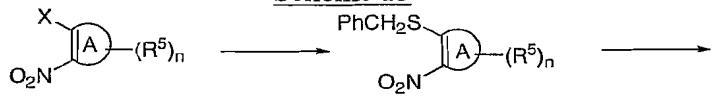


Compounds of formula (**12**) can be reacted with aqueous base solutions such as potassium hydroxide and the like under heated conditions to provide compounds of formula (**26**). Compounds of formula (**26**) can be reacted with a base in a solvent, or mixtures of solvents such as, but not limited to, N,N-dimethylformamide, tetrahydrofuran, diethyl ether, or methyl tert-butyl ether, and the like, followed by treatment with carbon disulfide at a temperature of about room temperature to about 70°C. Examples of the base include, but not limited to, sodium hydride, potassium hydride, lithium diisopropylamide, sodium hexamethyldisilazide and lithium hexamethyldisilazide. Subsequent treatment with a methylating reagent at a temperature of about 25°C provides compounds of formula (**27**). Examples of the methylating agent include, but not limited to, methyl iodide, methyl triflate, dimethylsulfate, and the like.

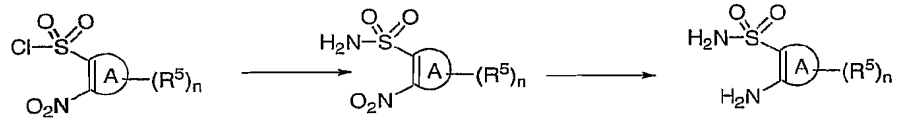
Alternatively, compounds of the formula (**26**) can be reacted with tris(methylthio)methyl methyl sulfate in the presence of a base in a solvent such as 1,4-dioxane or dimethylacetamide, and the like, at a temperature of about 25°C to about 150°C to give compounds of formula (**27**). Examples of the base include, but are not limited to, organic amine bases such as imidazole, 1-methylimidazole, 2-methylimidazole, 2-isopropylimidazole, 4-methylimidazole, 4-nitroimidazole, pyridine, N,N-dimethylaminopyridine, 1,2,4-triazole, pyrrole, 3-methylpyrrole, triethylamine, diisopropylethylamine or N-methylmorpholine and the like.

Compounds of formula (**27**) can be treated with compounds such as (**13**) in a solvent or a mixture of solvents, such as but not limited to, toluene, benzene, dioxane or tetrahydrofuran, and the like, at a temperature of about 50°C to about 150°C to provide compounds of formula (**11**).

Scheme 13



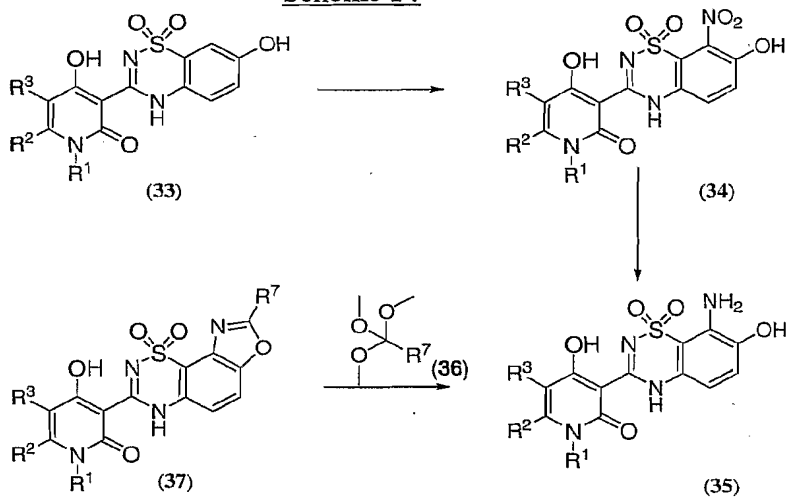
(29) (30)



(31) (32) (13)

Compounds of the formula (**29**) wherein X is I, Br, Cl or F can be treated with alkyl thiols such as benzene methylthiol in the presence of a base such as sodium carbonate in solvents such as ethanol and the like under heated conditions to give compounds of the formula (**30**). Treatment of (**30**) with chlorine gas in hydrochloric acid or acetic acid provides compounds of the formula (**31**). Compounds of the formula (**31**) in solvents such as but not limited to dichloromethane, tetrahydrofuran or dioxane can be treated with ammonia or ammonium hydroxide to give compounds of the formula (**32**). Reduction of compounds of the formula (**32**) with iron powder and ammonium chloride in aqueous alcoholic solvents such as methanol or ethanol under heated conditions optionally with iron powder in acetic acid under heated conditions to provide compounds of the formula (**13**).

Scheme 14

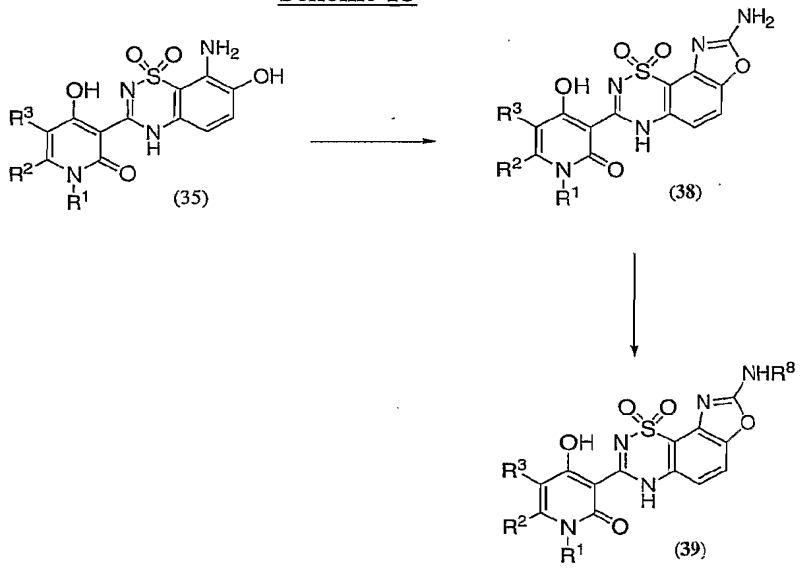


(33) (34) (37) (36) (35)

Compounds of the formula (**33**) can be treated with ammonium nitrate in the presence of a sulfuric acid as solvent under cooling conditions to give compounds of the formula (**34**). Reduction of compounds of the formula (**34**) with iron powder and ammonium chloride in

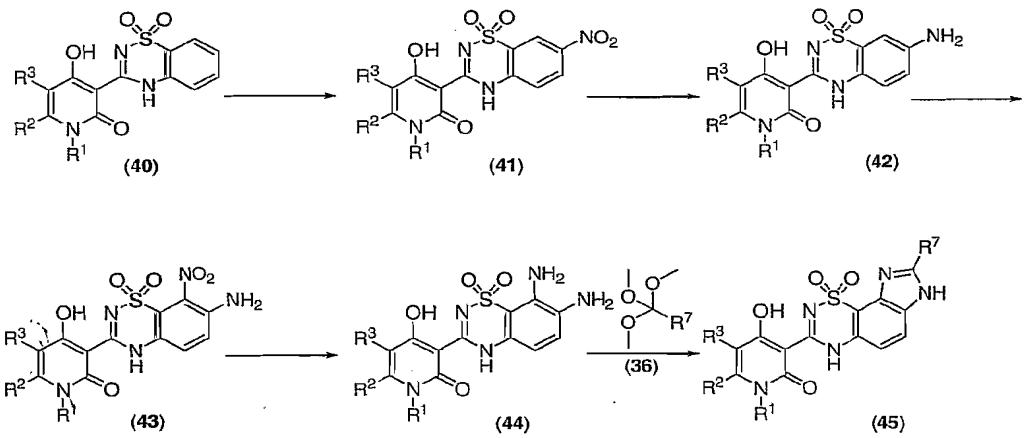
aqueous alcoholic solvents such as methanol or ethanol under heated conditions provides compounds of the formula (**35**). Alternatively, the reduction can also be achieved by treating compounds of formula (**35**) with iron powder in acids such as but not limited to acetic acid or dilute hydrochloric acid under heated conditions. Treatment of compounds of the formula (**35**) with an orthoester of the formula (**36**) under heating conditions to provide compounds of the formula (**37**).

Scheme 15



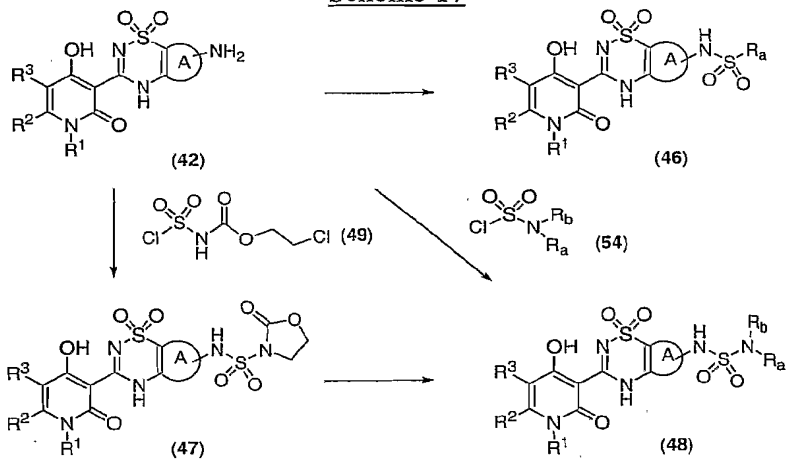
Compounds of the formula (**35**) can be treated with cyanogen bromide under heating conditions to give compounds of the formula (**38**). Treatment of compounds of the formula (**38**) with R^8X wherein X is Br, Cl, or I, R^8CO_2Cl, or R^8SO_2Cl in the presence of an amine base such as triethylamine, pyridine, or an inorganic base such as cesium carbonate or potassium carbonate in an appropriate solvent or a mixture of solvents selected from dimethylacetamide, N,N-dimethylformamide, methanol, dichloromethane, tetrahydrofuran, or acetonitrile and the like to provide compounds of the formula (**39**).

Scheme 16



Compounds of formula (**40**) can be nitrated with ammonium nitrate or potassium nitrate in the presence of an acid such as sulfuric acid, or trifluoroacetic acid in trifluoroacetic anhydride, with or without additional solvent, under cooling conditions to give compounds of the formula (**41**). Reduction of compounds of the formula (**41**) with iron powder and ammonium chloride in aqueous alcoholic solvents such as methanol or ethanol under heated conditions provides compounds of the formula (**42**). Alternatively, the reduction of compounds of formula (**42**) can also be accomplished using iron powder in acids such as but not limited to acetic acid or dilute hydrochloric acid under heated conditions. Compounds of the formula (**42**) can be converted to compounds of the formula (**44**) by (a) nitration and (b) reduction of the product of step (b), using the respective conditions as mentioned above. Compounds of the formula (**44**) can be treated with an orthoester of the formula (**36**) under heating conditions to provide compounds of the formula (**45**).

Scheme 17

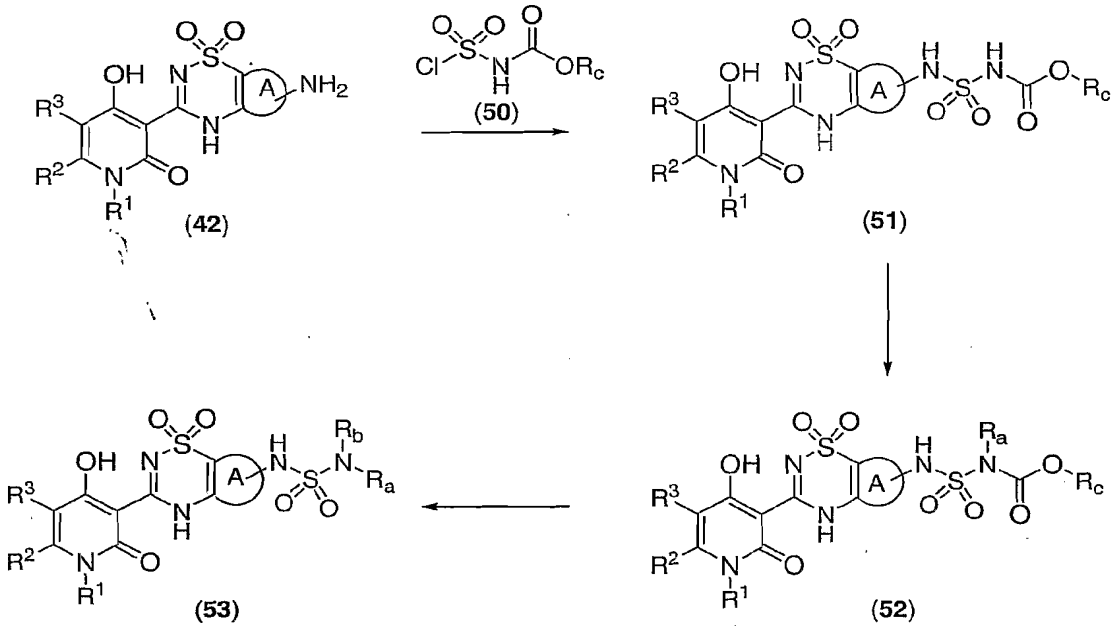


Compounds of formula (**42**) can be sulfonylated with a sulfonyl chloride of formula R_aSO_2Cl in the presence of a base such as pyridine alone or an amine base such as triethylamine, diisopropylethylamine, and the like in a solvent or combination of solvents

such as dichloromethane, tetrahydrofuran, or dioxane, to provide compounds of formula (**46**). Alternatively, compounds of formula (**42**) can be sulfamoylated in the presence of an amine base such as but not limited to triethylamine, or diisopropylethylamine, and the like, in a solvent or combination of solvents such as dichloromethane, tetrahydrofuran or dioxane, and the like, with compounds of formula (**49**) to give compounds of formula (**47**). Compounds of formula (**49**) can be obtained by treating chlorosulfonyl isocyanate and 2-chloroethanol in conditions that are well known in the art. Compounds of formula (**47**) can be treated further with an amine having the formula R_aR_bNH, (where R_a and R_b are as defined herein) in a solvent or combination of solvents such as dichloromethane, THF, or acetonitrile, and the like, under heating conditions to provide compounds of formula (**48**). Compounds of formula (**42**) can be sulfamoylated in the presence of an amine base such as triethylamine, or diisopropylethylamine, and the like, in a solvent or combination of solvents such as dichloromethane, tetrahydrofuran or dioxane, and the like, with compounds of formula (**54**) to give compounds of formula (**48**). Compounds of formula (**54**) can be obtained by treating an amine of the formula R_aR_bNH with sulfuryl chloride or by (a) treating an amine of the formula R_aR_bNH with chlorosulfonic acid, and (b) contacting the product of step (a) with a chlorinating agent such as phosphorous pentachloride and the like in conditions that are well known in the art.

Similarly, compounds of formula (**11**) wherein R^5 is -alkylNH_2 can be converted to compounds of formula (**11**) wherein R^5 is -alkyl$NHSO_2NR_aR_b$ using the conditions for the transformation of compounds of formula (**42**) to compounds of formula (**48**). Compounds of formula (**11**) wherein R^5 is -alkylNH_2 can be converted to compounds of formula (**11**) wherein R^5 is –alkyl$NHSO_2R_a$ can be achieved by employing the conditions for the transformation of compounds of formula (**42**) to compounds of formula (**46**).

Scheme 18



Compounds of formula (**42**) can be sulfamoylated with a sulfamoyl chloride of formula $R_cOC(O)NHSO_2Cl$ (**50**), in the presence of an amine base such as pyridine, triethylamine or diisopropylethylamine, and the like, in a solvent or combination of solvents such as dichloromethane, tetrahydrofuran, diethyl ether, benzene, or acetonitrile, and the like, to provide compounds of formula (**51**). Compounds of formula (**50**) can be prepared by treating an alcohol of formula R_cOH with chlorosulfonyl isocyanate in a solvent or combination of solvents such as dichloromethane, carbon tetrachloride, diethyl ether, benzene, or toluene, and the like. Compounds of formula (**51**) can be treated further with an alcohol having the formula R_aOH in the presence of tri-*n*-butylphosphine or triphenylphosphine, and the like, and diisopropylazodicarboxylate, 1,1'-(azadicarbonyl)piperidine, or diethylazodicarboxylate, and the like, in a solvent or combination of solvents such as dichloromethane or tetrahydrofuran to provide compounds of formula (**52**). Alternatively, compounds of formula (**52**) wherein R_a is methyl can be obtained by methylating compounds of formula (**51**) with a methylating agent such as, but not limited to, methyl iodide, dimethyl sulfate, trimethysilyldiazomethane in conditions that are well known in the art. Transformation of compounds of formula (**52**) to compounds of formula (**53**) can be achieved by reaction with an acid such as trifluoroacetic acid or hydrochloric acid, or by hydrogenolysis conditions such as palladium on carbon under hydrogen gas.

Similarly, compounds of formula (**11**) wherein R^5 is $-alkylNH_2$ can be converted to compounds of formula (**11**) wherein R^5 is $-alkylNHSO_2NHCOOR_c$ by the conditions for the

transformation of compounds of formula (**42**) to compounds of formula (**51**).

Compounds of formula (**11**) wherein R^5 is –alkylNH$_2$ can be converted to compounds of formula (**11**) wherein R^5 is –alkylNHSO$_2$N(R_a)COOR_c by the conditions employed for the conversion of (**51**) to (**52**).

Compounds of formula (**11**) wherein R^5 is –alkylNH$_2$ can be converted to compounds of formula (**11**) wherein R^5 is –alkylNHSO$_2$NR_aR_b by the conditions employed for the conversion of (**52**) to (**53**).

The present invention will now be described in connection with certain preferred embodiments which are not intended to limit its scope. On the contrary, the present invention covers all alternatives, modifications, and equivalents as can be included within the scope of the claims. Thus, the following examples, which include preferred embodiments, will illustrate the preferred practice of the present invention, it being understood that the examples are for the purpose of illustration of certain preferred embodiments and are presented to provide what is believed to be the most useful and readily understood description of its procedures and conceptual aspects.

Compounds of the invention were named by ACD/ChemSketch version 5.0 (developed by Advanced Chemistry Development, Inc., Toronto, ON, Canada) or were given names consistent with ACD nomenclature.

Example 1

1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 1A

2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared from 2,3–pyridinecarboxylic anhydride (11.4 g, 76 mmol) and trimethylsilyl azide (11.0 mL, 80 mmol) according to the procedure described in *Synthesis*, **1982**, 972-973 as a white solid (7.27 g, 58%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.31 (dd, *J*=7.72, 4.78 Hz, 1H), 8.31 (dd, *J*=7.72, 1.84 Hz, 1H), 8.66 (dd, *J*=4.78, 1.84 Hz, 1H), 12.27 (s, 1H).

Example 1B

1-butyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

A suspension of sodium hydride (95%, 0.96 g, 40 mmol) in dimethylacetamide (60 mL) at 10 °C under nitrogen was reacted with the product of Example 1A (5.7 g, 34.7 mmol) with stirring for 1 hour then treated with n-butylbromide (5.2 g, 38 mmol) and stirred for an additional 16 hours. The reaction was partitioned between ethyl acetate and water. The organic layer was washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum. The crude product was purified by flash column chromatography with silica gel eluting with hexane and ethyl acetate (3:1) to give the title

compound as a white solid, (2.5 g, 33% yield). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.92 (t, *J*=7.35 Hz, 3H), 1.36 (m, 2H), 1.65 (m, 2H), 4.13 (m, 2H), 7.38 (dd, *J*=7.72, 4.78 Hz, 1H), 8.39 (dd, *J*=7.72, 1.84 Hz, 1H), 8.77 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 1C

ethyl (1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)acetate

The title compound was prepared as a white solid in two steps (46% yield) from 2-aminobenzenesulfonamide according to the procedure described in *Chemistry of Heterocyclic Compounds* (English Translation), **1998**, *34*(7), 791-795. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.21 (t, *J*=7.17 Hz, 3H), 4.16 (q, *J*=7.23 Hz, 2H), 7.32 (d, *J*=7.35 Hz, 1H), 7.47 (m, 1H), 7.69 (m, 1H), 7.82 (dd, *J*=7.91, 1.29 Hz, 1H), 12.27 (s, 1H).

Example 1D

1-butyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

To a solution of the product of Example 1B (0.220 g, 1.0 mmol) and the product of Example 1C (0.268 g, 1.0 mmol) in anhydrous THF (10 mL) under nitrogen at 0 °C was added sodium hydride (95%, 0.10 g, 4.0 mmol). The reaction was heated to reflux for 3 hours, cooled to 0 °C, and to it was added dropwise glacial acetic acid (2 mL). The resulting mixture was heated to reflux for 2 hours, cooled to ambient temperature, and diluted with aqueous hydrochloric acid (0.1 M, 10 mL). The resulting precipitate was collected by filtration, washed with water and diethyl ether and dried to give the title compound (0.130 g, 33%). MS (ESI-) m/z 397 $(M-H)^-$.

A stirred suspension of the title compound (0.130 g, 0.326 mmol) in acetonitrile and water (1:1, 4 mL) was reacted with aqueous sodium hydroxide (1 M, 0.326 mL, 0.326 mmol), for approximately 30 minutes when a clear solution was observed. The solution was lyophilized to give the sodium salt. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.92 (t, *J*=7.35 Hz, 3H), 1.35 (m, 2H), 1.58 (m, 2H), 4.28 (t, *J*=7.35 Hz, 2H), 7.13 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.55 (m, 1H), 7.66 (dd, *J*=7.72, 1.47 Hz, 1H), 8.37 (dd, *J*=7.72, 1.84 Hz, 1H), 8.53 (dd, *J*=4.60, 2.02 Hz, 1H), 15.92 (s, 1H).

Example 2

1-[(5-chloro-2-thienyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 2A

1-[(5-chloro-2-thienyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-chloro-5-chloromethylthiophene for n-butyl bromide (0.195 g, 52%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.38 (s, 2H), 6.98 (d, *J*=4.04 Hz, 1H), 7.08 (d, *J*=3.68 Hz, 1H), 7.43

(dd, J=7.72, 4.78 Hz, 1H), 8.41 (dd, J=7.72, 1.84 Hz, 1H), 8.83 (dd, J=4.78, 1.84 Hz, 1H).

Example 2B

1-[(5-chloro-2-thienyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 2A for the product of Example 1B (0.167 g, 58%). MS (ESI-) m/z 471/473 $(M-H)^-$.

The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.53 (s, 2H), 6.89 (d, J=3.68 Hz, 1H), 7.00 (d, J=3.68 Hz, 1H), 7.20 (dd, J=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (t, J=7.72 Hz, 1H), 7.67 (d, J=7.72 Hz, 1H), 8.40 (dd, J=7.72, 1.84 Hz, 1H), 8.58 (dd, J=4.78, 1.84 Hz, 1H), 15.73 (s, 1H).

Example 3

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(2-ethylbutyl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 3A

ethyl 2-[(2-ethylbutyl)amino]nicotinate

Ethyl 2-chloronicotinate (0.646 g, 3.48 mmol) and 2-ethylbutylamine (0.74 g, 7.31 mmol) were reacted in a sealed tube at 130 °C for 2 hours. The reaction mixture was partitioned between dichloromethane and water. The aqueous layer was extracted with dichloromethane (2 x 50 mL). The organic layers were combined and dried over magnesium sulfate, filtered, and concentrated. The residue was purified by column chromatography on silica gel eluting with hexane/ethyl acetate (19:1) to provide the title compound (0.665 g, 76%). MS (ESI+) m/z 251.1 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J=7.54 Hz, 6H), 1.41 (m, 7H), 1.55 (m, 1H), 3.46 (m, 2H), 4.32 (q, J=6.99 Hz, 2H), 6.48 (dd, J=7.72, 4.78 Hz, 1H), 7.99 (s, 1H), 8.11 (dd, J=7.72, 2.21 Hz, 1H), 8.27 (dd, J=4.78, 1.84 Hz, 1H).

Example 3B

1-(2-ethylbutyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The product of Example 3A (0.664 g, 2.65 mmol) and diphosgene (1.57 g, 7.96 mmol) in 13 mL of 1,2-dichloroethane and 1.3 mL of 1,4 dioxane were reacted at 80 °C for 16 hours. The reaction was concentrated under vacuum and the residue was purified by flash column chromatography on silica gel eluting with hexane/ethyl acetate (9:1) to provide the title compound (0.235 g, 36 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (m, 6H), 1.40 (m, 4H), 1.52 (m, 2H), 4.21 (m, 1H), 7.25 (m, 1H), 8.41 (dd, J=7.72, 1.84 Hz, 1H), 8.70 (dd, J=4.78, 1.84 Hz, 1H).

Example 3C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(2-ethylbutyl)-4-hydroxy-1,8-naphthyridin-

2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 3B for the product of Example 1B (0.041 g, 38 %). MS (ESI+) m/z 427.1 $(M+H)^+$, (ESI-) m/z 425.1 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.87 (t, *J*=7.54 Hz, 6H), 1.30 (m, 4H), 1.99 (m, 1H), 4.44 (d, *J*=7.35 Hz, 2H), 7.49 (dd, *J*=7.72, 4.78 Hz, 1H), 7.55 (t, *J*=7.35 Hz, 1H), 7.68 (d, *J*=8.09 Hz, 1H), 7.77 (t, *J*=7.17 Hz, 1H), 7.92 (d, *J*=8.09 Hz, 1H), 8.57 (dd, *J*=7.72, 1.84 Hz, 1H), 8.86 (d, *J*=4.78 Hz, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI+) m/z 427.1 $(M+H)^+$, (ESI-) m/z 425.1 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.86 (t, *J*=7.35 Hz, 6H), 1.28 (m, 4H), 1.91 (m, 1H), 4.25 (d, *J*=7.35 Hz, 2H), 7.12 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.55 (m, 1H), 7.67 (dd, *J*=8.09, 1.47 Hz, 1H), 8.37 (dd, *J*=7.72, 1.84 Hz, 1H), 8.50 (dd, *J*=4.60, 2.02 Hz, 1H), 15.97 (s, 1H).

Example 4

1-[(5-bromo-2-thienyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 4A

1-[(5-bromo-2-thienyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-bromo-5-chloromethylthiophene for n-butyl bromide (0.229 g, 55%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.40 (s, 2H), 7.06 (m, 2H), 7.43 (dd, *J*=7.72, 4.78 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.83 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 4B

1-[(5-bromo-2-thienyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 4A for the product of Example 1B (0.208 g, 60%). MS (ESI-) m/z 515/517 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.55 (s, 2H), 6.97 (d, *J*=3.68 Hz, 1H), 7.00 (d, *J*=3.68 Hz, 1H), 7.20 (dd, *J*=7.73, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (m, 1H), 7.68 (d, *J*=7.72 Hz, 1H), 8.40 (dd, *J*=7.72, 2.21 Hz, 1H), 8.58 (dd, *J*=4.78, 2.20 Hz, 1H), 15.73 (s, 1H).

Example 5

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-methylbenzyl)-1,8-naphthyridin-2(1H)-one

Example 5A

1-(3-methylbenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B

substituting 3-methylbenzyl bromide for n-butyl bromide (0.305 g, 62%). MS (DCI) m/z 269 $(M+H)^+$.

Example 5B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-methylbenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 5A for the product of Example 1B (0.112 g, 72%). MS (ESI-) m/z 445 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.23 (s, 3H), 5.48 (s, 2H), 7.01 (m, 3H), 7.14 (t, J=7.35 Hz, 2H), 7.28 (m, 2H), 7.56 (td, J=7.72, 1.47 Hz, 1H), 7.67 (dd, J=7.72, 1.47 Hz, 1H), 8.41 (dd, J=7.72, 1.84 Hz, 1H), 8.48 (dd, J=4.78, 1.84 Hz, 1H), 15.86 (s, 1H).

Example 6

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-nitrobenzyl)-1,8-naphthyridin-2(1H)-one

Example 6A

1-(3-nitrobenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-nitrobenzyl bromide for n-butyl bromide (0.147 g, 28%). MS (DCI) m/z 300 $(M+H)^+$.

Example 6B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-nitrobenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 6A for the product of Example 1B (0.032 g, 42%). MS (ESI-) m/z 476 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.62 (s, 2H), 7.19 (dd, J=7.72, 4.78 Hz, 1H), 7.29 (td, J=8.36, 1.29 Hz, 2H), 7.56 (t, J=8.46 Hz, 1H), 7.58 (t, J=7.72 Hz, 1H), 7.67 (d, J=8.09 Hz, 1H), 7.74 (d, J=8.09 Hz, 1H), 8.08 (m, 2H), 8.43 (dd, J=7.54, 2.02 Hz, 1H), 8.50 (dd, J=4.60, 2.02 Hz, 1H), 15.76 (s, 1H).

Example 7

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-thienylmethyl)-1,8-naphthyridin-2(1H)-one

Example 7A

1-(3-thienylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-(bromomethyl)thiophene for n-butyl bromide (0.170 g, 52%). ^{1}H NMR (300

MHz, DMSO-d_6) δ 5.32 (s, 2H), 7.15 (m, 1H), 7.40 (dd, *J*=7.72, 4.78 Hz, 1H), 7.48 (m, 2H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.76 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 7B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-thienylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 7A for the product of Example 1B (0.135 g, 48%). MS (ESI-) m/z 437 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.48 (s, 2H), 7.09 (d, *J*=4.04 Hz, 1H), 7.16 (dd, *J*=7.72, 4.78 Hz, 1H), 7.27 (m, 3H), 7.38 (dd, *J*=4.96, 3.13 Hz, 1H), 7.56 (t, *J*=7.72 Hz, 1H), 7.67 (d, *J*=8.09 Hz, 1H), 8.39 (dd, *J*=7.72, 1.66 Hz, 1H), 8.53 (dd, *J*=4.78, 1.66 Hz, 1H), 15.85 (s, 1H).

Example 8

1-(3-chlorobenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 8A

1-(3-chlorobenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-chlorobenzyl bromide for n-butyl bromide (0.405 g, 77%). MS (DCI) m/z 289 $(M+H)^+$.

Example 8B

1-(3-chlorobenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 8A for the product of Example 1B (0.050 g, 45%). MS (ESI-) m/z 465 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d6) δ 5.50 (s, 2 H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1 H), 7.27 (m, 6 H), 7.56 (td, *J*=7.91, 1.47 Hz, 1 H), 7.67 (d, *J*=7.72 Hz, 1 H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1 H), 8.49 (dd, *J*=4.78, 2.21 Hz, 1 H), 15.78 (s, 1 H).

Example 9

1-(3-bromobenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 9A

1-(3-bromobenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-bromobenzyl bromide for n-butyl bromide (0.500 g, 82%). MS (DCI) m/z 333 $(M+H)^+$.

Example 9B

1-(3-bromobenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 9A for the product of Example 1B (0.050 g, 45%). MS (ESI-) m/z 465 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.50 (s, 2H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.27 (m, 6H), 7.56 (td, *J*=7.91, 1.47 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.78, 2.21 Hz, 1H), 15.78 (s, 1H).

Example 10

1-[(2-chloro-1,3-thiazol-5-yl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 10A

1-[(2-chloro-1,3-thiazol-5-yl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-chloro-5-bromomethylthiazole for n-butyl bromide (0.360 g, 60%). MS (APCI) m/z 296 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.45 (s, 2H), 7.44 (dd, *J*=7.72, 4.78 Hz, 1H), 7.76 (s, 1H), 8.42 (dd, *J*=7.91, 1.65 Hz, 1H), 8.82 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 10B

1-[(2-chloro-1,3-thiazol-5-yl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 10A for the product of Example 1B (0.136 g, 60%). MS (ESI-) m/z 477 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.76 (s, 2H), 7.56 (m, 2H), 7.65 (d, *J*=7.35 Hz, 1H), 7.77 (s, 1H), 7.78 (m, 1H), 7.92 (d, *J*=8.09 Hz, 1H), 8.59 (dd, *J*=8.09, 1.84 Hz, 1H), 8.92 (dd, *J*=4.78, 1.84 Hz, 1H), 13.72 (s, 1H).

Example 11

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(3-fluorobenzyl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 11A

1-(3-fluorobenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-fluorobenzyl bromide for n-butyl bromide (0.382 g, 76%). MS (DCI) m/z 273 $(M+H)^+$.

Example 11B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(3-fluorobenzyl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 11A for the product of Example 1B (0.040 g, 37%). MS (ESI-) m/z 449 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 5.52 (s, 2H), 7.02 (m, 2H), 7.08 (d, *J*=7.72 Hz, 1H), 7.17 (dd, *J*=7.72, 4.41 Hz, 1H), 7.29 (m, 3H), 7.56 (td, *J*=7.91, 1.47 Hz, 1H), 7.67 (d, *J*=8.09 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.78, 1.84 Hz, 1H), 15.79 (s, 1H).

Example 12

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one

Example 12A

1-(3-methylbutyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

A suspension of sodium hydride (95%, 0.048 g, 2.0 mmol) in dimethylacetamide (2 mL) at 20°C under nitrogen was reacted with the product of Example 1A (0.3 g, 1.83 mmol). The reaction mixture was stirred for 1/2 hour then treated with 1-bromo-3-methylbutane (0.3 g, 2.0 mmol) and stirred for an additional 16 hours. The reaction was partitioned between ethyl acetate and water. The organic layer was washed with water and brine, dried over sodium sulfate, filtered and concentrated under vacuum. The crude product was purified by flash column chromatography on silica gel eluting with hexanes and ethyl acetate (3:1) to give the title compound as a white solid (0.218 g, 51%). MS (ESI-) m/z 233 $(M-H)^-$. ^1H NMR (300 MHz, DMSO-d_6) δ 0.93 (s, 3H), 0.96 (s, 3H), 1.55 (m, 2H), 1.66 (m, 1H), 4.14 (t, *J*=7.72 Hz, 2H), 7.37 (dd, *J*=7.91, 4.96 Hz, 1H), 8.38 (dd, *J*=7.72, 1.84 Hz, 1H), 8.78 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 12B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-methylbutyl)-1,8-naphthyridin-2(1H)-one

To a solution of the product of Example 12A (0.216 g, 0.92 mmol) and the product of Example 1C (0.247 g, 0.922 mmol) in anhydrous THF (7.5 mL) under nitrogen at 20°C was added sodium hydride (95%, 0.089 g, 3.7 mmol). The reaction was heated at reflux for 3 hours, cooled to 20°C, and added dropwise glacial acetic acid (2.4 mL). The resulting mixture was heated at reflux for 1 hour, cooled to 25°C, and diluted with aqueous hydrochloric acid (0.5 M, 35 mL). The resulting precipitate was collected by filtration, washed with water and dried. The crude product was purified by flash column chromatography on silica gel eluting with hexanes and ethyl acetate (3:1) to give the title compound as a white solid (0.031 g, 20%). MS (ESI-) m/z 411 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 411 $(M-H)^-$. ^1H NMR (300 MHz, DMSO-d_6) δ 0.95 (s, 3H), 0.98 (s, 3H), 1.47 (m, 2H), 1.64

(m, 1H), 4.30 (t, *J*=7.72 Hz, 2H), 7.13 (dd, *J*=7.72, 4.78 Hz, 1H), 7.26 (d, *J*=8.09 Hz, 1H), 7.30 (d, *J*=7.72 Hz, 1H), 7.55 (t, *J*=7.72 Hz, 1H), 7.66 (d, *J*=8.09 Hz, 1H), 8.37 (dd, *J*=7.72, 1.84 Hz, 1H), 8.53 (dd, *J*=4.78, 2.21 Hz, 1H), 15.94 (s, 1H).

Example 13

1-(cyclobutylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 13A

1-(cyclobutylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting bromomethyl-cyclobutane for n-butyl bromide (0.255 g, 60%). MS (DCI) m/z 233 $(M+H)^+$.

Example 13B

1-(cyclobutylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 13A for the product of Example 1B (0.120 g, 52%). MS (ESI-) m/z 409 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.83 (m, 6H), 2.79 (m, 1H), 4.38 (d, *J*=6.99 Hz, 2H), 7.13 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (t, *J*=7.54 Hz, 2H), 7.55 (t, *J*=7.72 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.36 (dd, *J*=7.72, 2.21 Hz, 1H), 8.51 (dd, *J*=4.78, 1.84 Hz, 1H), 15.92 (s, 1H).

Example 14

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-methyl-2-thienyl)methyl]-1,8-naphthyridin-2(1H)-one

Example 14A

1-[(5-methyl-2-thienyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-bromomethyl-5-methylthiophene for n-butyl bromide (0.181 g, 54%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.36 (s, 3H), 5.38 (s, 2H), 6.63 (m, 1H), 6.98 (d, *J*=3.68 Hz, 1H), 7.42 (dd, *J*=7.72, 4.78 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.82 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 14B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-methyl-2-thienyl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 14A for the product of Example 1B (0.172 g, 58%). MS (ESI-) m/z 451 $(M-H)^-$. The sodium salt of the title compound was prepared according to the

procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.32 (s, 3H), 5.54 (s, 2H), 6.56 (d, 1H), 6.88 (d, *J*=3.31 Hz, 1H), 7.17 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.56 (t, *J*=7.72 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.38 (dd, *J*=7.72, 1.84 Hz, 1H), 8.56 (dd, *J*=4.78, 1.84 Hz, 1H), 15.81 (s, 1H).

Example 15

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 15A

1-benzyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting benzyl bromide for n-butyl bromide (0.393 g, 51%). MS (DCI) m/z 255 $(M+H)^+$.

Example 15B

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 15A for the product of Example 1B (0.217 g, 62%). MS (ESI-) m/z 431 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.52 (s, 2H), 7.16 (m, 2H), 7.25 (d, *J*=4.41 Hz, 4H), 7.29 (m, 2H), 7.56 (td, *J*=7.91, 1.47 Hz, 1H), 7.67 (dd, *J*=7.91, 1.65 Hz, 1H), 8.41 (dd, *J*=7.54, 2.02 Hz, 1H), 8.48 (dd, *J*=4.78, 2.21 Hz, 1H), 15.84 (s, 1H).

Example 16

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-methyl-3-pyridinyl)methyl]-1,8-naphthyridin-2(1H)-one

Example 16A

1-[(5-methyl-3-pyridinyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-chloromethyl-5-methylpyridine for n-butyl bromide (0.080 g, 24%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.25 (s, 3H), 5.34 (s, 2H), 7.40 (dd, *J*=7.72, 4.78 Hz, 1H), 7.63 (br s, 1H), 8.30 (br s, 1H), 8.43 (dd, *J*=7.72, 1.84 Hz, 1H), 8.46 (br s, 1H), 8.73 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 16B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-methyl-3-pyridinyl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 16A for the product of Example 1B (0.013 g, 13%). MS (ESI-) m/z 446 $(M-H)^-$. The sodium salt of the title compound was prepared according to the

procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.22 (s, 3H), 5.49 (s, 2H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.44 (s, 1H), 7.56 (m, 1H), 7.67 (d, *J*=8.09 Hz, 1H), 8.23 (d, *J*=1.47 Hz, 1H), 8.36 (d, *J*=1.47 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.51 (dd, *J*=4.78, 1.84 Hz, 1H), 15.80 (s, 1H).

Example 17

1-[(2-chloro-4-pyridinyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 17A

1-[(2-chloro-4-pyridinyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-bromomethyl-2-chloropyridine for n-butyl bromide (0.219 g, 62%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.37 (s, 2H), 7.40 (m, 1H), 7.48 (s, 1H), 7.60 (s, 1H), 8.34 (dd, *J*=4.60, 2.39 Hz, 1H), 8.45 (m, 1H), 8.68 (m, 1H).

Example 17B

1-[(2-chloro-4-pyridinyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 17A for the product of Example 1B (0.255 g, 73%). MS (ESI-) m/z 466/468 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.52 (s, 2H), 7.19 (m, 2H), 7.30 (m, 3H), 7.56 (t, *J*=7.54 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.27 (d, *J*=5.15 Hz, 1H), 8.46 (m, 2H), 15.72 (s, 1H).

Example 18

1-[(5-bromo-3-pyridinyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 18A

di-tert-butyl (5-bromo-3-pyridinyl)methylimidodicarbonate

A solution of 5-bromo-3-chloromethylpyridinium hydrochloride (716 mg, 4.189 mmol) in anhydrous DMF (15 mL) under nitrogen at 0 °C was treated with triethylamine (0.65 mL, 4.61 mmol), tetrabutylammonium bromide (273 mg, 0.838 mmol), and potassium di-tert-butyl imidodicarbonate (1.284 g, 5.027 mmol). The reaction was heated to 50 °C-55 °C for 3.5 hours, then cooled to room temperature, diluted with ethyl acetate (150 mL), and washed with water (2x50 mL) and saturated aqueous sodium chloride. The combined extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation. The residue was purified by flash column chromatography on silica gel with 6% ethyl acetate/dichloromethane to give the title compound as a colorless oil (0.980 g, 60%). MS

(ESI+) m/z 387/389 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 (s, 18H), 4.75 (s, 2H), 7.83 (t, *J*=2.02 Hz, 1H), 8.50 (d, *J*=1.84 Hz, 1H), 8.58 (d, *J*=2.21 Hz, 1H).

Example 18B

(5-bromo-3-pyridinyl)methylamine

The product of Example 18A (0.98 g, 2.53 mmol) was treated with trifluoroacetic acid and dichloromethane (1:1 v/v, 20 mL) for 2 hours at room temperature. The solvent was removed by rotary evaporation and the resulting oil was chased with benzene/dichloromethane (3 times) to give a waxy solid. The salt was dissolved in anhydrous methanol (20 mL) and stirred with Amberlite IRA-400(OH), resin (10 g) for 2 hrs. The resin was removed by vacuum filtration and thoroughly washed with dry methanol. The filtrate was concentrated by rotary evaporation to give the title compound (0.415 g, 88%). MS (DCI/NH_3) m/z 187/189 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 3.73 (s, 2H), 8.02 (t, *J*=2.02 Hz, 1H), 8.50 (d, *J*=1.47 Hz, 1H), 8.53 (d, *J*=2.21 Hz, 1H).

Example 18C

ethyl 2-{[(5-bromo-3-pyridinyl)methyl]amino}nicotinate

The title compound was prepared according to the procedure of Example 3A substituting the product of Example 18B for 2-ethylbutylamine (0.116 g, 68%). MS (DCI/NH_3) m/z 336/338 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 1.32 (t, *J*=6.99 Hz, 3H), 4.31 (q, *J*=7.23 Hz, 2H), 4.71 (d, *J*=5.88 Hz, 2H), 6.67 (dd, *J*=7.72, 4.78 Hz, 1H), 7.97 (t, *J*=2.02 Hz, 1H), 8.12 (dd, *J*=7.72, 2.21 Hz, 1H), 8.26 (dd, *J*=4.78, 1.84 Hz, 1H), 8.45 (t, *J*=6.07 Hz, 1H), 8.55 (m, 2H).

Example 18D

1-[(5-bromo-3-pyridinyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 18C for the product of Example 3A and purifying by flash column chromatography on silica gel eluting with 10% ethyl acetate/dichloromethane (0.057 g, 51%). ^1H NMR (300 MHz, DMSO-d_6) δ 5.38 (s, 2H), 7.41 (dd, *J*=7.72, 5.15 Hz, 1H), 8.10 (t, *J*=2.02 Hz, 1H), 8.43 (dd, *J*=7.72, 1.84 Hz, 1H), 8.60 (d, *J*=2.21 Hz, 1H), 8.66 (d, *J*=1.84 Hz, 1H), 8.72 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 18E

1-[(5-bromo-3-pyridinyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 18D for the product of Example 1B (0.037 g, 43%). MS (ESI-) m/z 510/512 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 5.52 (s, 2H), 7.20 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (t, *J*=7.54 Hz, 1H), 7.68 (d, *J*=7.35 Hz, 1H), 7.89

(br s, 1H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.52 (dd, *J*=4.78, 1.84 Hz, 1H), 8.55 (br s, 2H), 15.73 (s, 1H).

Example 19

1-(cyclohexylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 19A

1-(cyclohexylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting (bromomethyl)cyclohexane for n-butyl bromide (0.05 g, 11%).

Example 19B

1-(cyclohexylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 19A for the product of Example 1B (0.025 g, 30 %). MS (ESI-) m/z 437 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 437 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6/TFA) δ 0.99 (m, 5H), 1.50 (m, 5H), 1.87 (m, 1H), 4.32 (d, *J*=7.35 Hz, 2H), 7.23 (dd, *J*=8.09, 4.78 Hz, 1H), 7.38 (m, 2H), 7.57 (m, 1H), 7.78 (d, *J*=8.09 Hz, 1H), 8.40 (dd, *J*=8.09, 1.84 Hz, 1H), 8.66 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 20

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2S)-2-methylbutyl]-1,8-naphthyridin-2(1H)-one

Example 20A

ethyl 2-{[(2S)-2-methylbutyl]amino}nicotinate

The title compound was prepared according to the procedure of Example 3A substituting (S)-(-)-2-methylbutylamine for 2-ethylbutylamine (1.6 g, 77%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.89 (t, *J*=7.23, 3H), 0.91 (d, *J*=6.62 Hz, 3H), 1.18 (m, 1H), 1.31 (t, *J*=6.99 Hz, 3H), 1.42 (m, 1H), 1.66 (m, 1H), 3.35 (m, 2H), 4.29 (q, *J*=7.23 Hz, 2H), 6.59 (dd, *J*=7.72, 4.78 Hz, 1H), 8.01 (t, *J*=5.52 Hz, 1H), 8.08 (dd, *J*=7.72, 1.84 Hz, 1H), 8.27 (dd, *J*=4.60, 2.02 Hz, 1H).

Example 20B

1-[(2S)-2-methylbutyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 20A for the product of Example 3A (0.400 g, 68%). MS (DCI) m/z 252 $(M+NH_4)^+$.

Example 20C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2S)-2-methylbutyl]-1,8-

naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 20B for the product of Example 1B (0.116 g, 43%). MS (ESI-) m/z 411 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.80 (d, J=6.99 Hz, 3H), 0.87 (t, J=7.54 Hz, 3H), 1.15 (m, 1H), 1.37 (m, 1H), 2.02 (m, 1H), 4.20 (d, J=7.35 Hz, 2H), 7.12 (dd, J=7.72, 4.78 Hz, 1H), 7.27 (m, 2H), 7.55 (m, 1H), 7.66 (d, J=7.72 Hz, 1H), 8.37 (dd, J=7.72, 2.21 Hz, 1H), 8.51 (dd, J=4.60, 2.02 Hz, 1H), 15.95 (s, 1H).

Example 21

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-methylbenzyl)-1,8-naphthyridin-2(1H)-one

Example 21A

1-(4-methylbenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-methylbenzyl bromide for n-butyl bromide (0.402 g, 82%). MS (DCI) m/z 269 $(M+H)^+$.

Example 21B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-methylbenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 21A for the product of Example 1B (0.099 g, 60%). MS (ESI-) m/z 445 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.22 (s, 3H), 5.47 (s, 2H), 7.04 (d, J=7.72 Hz, 2H), 7.14 (m, 3H), 7.29 (t, J=7.35 Hz, 2H), 7.55 (t, J=7.72 Hz, 1H), 7.67 (d, J=7.72 Hz, 1H), 8.39 (dd, J=7.72, 1.84 Hz, 1H), 8.48 (dd, J=4.78, 1.84 Hz, 1H), 15.85 (s, 1H).

Example 22

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-nitro-2-furyl)methyl]-1,8-naphthyridin-2(1H)-one

Example 22A

1-[(5-nitro-2-furyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-bromomethyl-5-nitrofuran for n-butyl bromide (0.120 g, 34%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.45 (s, 2H), 6.90 (d, J=3.68 Hz, 1H), 7.44 (dd, J=7.72, 5.15 Hz, 1H), 7.65 (d, J=3.68 Hz, 1H), 8.45 (m, 1H), 8.77 (m, 1H).

Example 22B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-nitro-2-furyl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 21A for the product of Example 1B (0.040 g, 21%). MS (DCI/NH_3) m/z 468 $(M+H)^+$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.60 (s, 2H), 6.54 (d, *J*=3.68 Hz, 1H), 7.22 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (m, 1H), 7.58 (d, *J*=3.68 Hz, 1H), 7.67 (d, *J*=8.09 Hz, 1H), 8.43 (dd, *J*=7.72, 1.84 Hz, 1H), 8.53 (dd, *J*=4.78, 1.84 Hz, 1H), 15.68 (s, 1H).

Example 23

1-(1-benzothien-2-ylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 23A

1-(1-benzothien-2-ylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-chloromethyl-benzo[b]thiophene for n-butyl bromide (0.160 g, 42%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.58 (s, 2H), 7.33 (m, 2H), 7.44 (dd, *J*=7.72, 4.78 Hz, 1H), 7.51 (s, 1H), 7.77 (m, 1H), 7.90 (m, 1H), 8.44 (dd, *J*=7.72, 1.84 Hz, 1H), 8.83 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 23B

1-(1-benzothien-2-ylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 23A for the product of Example 1B (0.148 g, 60%). MS (ESI-) m/z 487 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.74 (s, 2H), 7.20 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 4H), 7.36 (s, 1H), 7.56 (m, 1H), 7.68 (dd, *J*=7.72, 1.47 Hz, 1H), 7.75 (m, 1H), 7.82 (dd, *J*=7.72, 1.47 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.58 (dd, *J*=4.78, 1.84 Hz, 1H), 15.77 (s, 1H).

Example 24

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-methoxybenzyl)-1,8-naphthyridin-2(1H)-one

Example 24A

1-(3-methoxybenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-methoxybenzyl bromide for n-butyl bromide (0.446 g, 86%). MS (DCI) m/z

285 $(M+H)^+$.

Example 24B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-methoxybenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 24A for the product of Example 1B (0.086 g, 53%). MS (ESI-) m/z 461 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.69 (s, 3H), 5.49 (s, 2H), 6.75 (m, 3H), 7.15 (m, 2H), 7.29 (td, *J*=8.46, 1.84 Hz, 2H), 7.56 (td, *J*=7.72, 1.47 Hz, 1H), 7.66 (d, *J*=7.72 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.48 (dd, *J*=4.78, 1.84 Hz, 1H), 15.82 (s, 1H).

Example 25

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-iodobenzyl)-1,8-naphthyridin-2(1H)-one

Example 25A

1-(3-iodobenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-iodobenzyl bromide for n-butyl bromide (0.614 g, 88%). MS (DCI) m/z 381 $(M+H)^+$.

Example 25B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-iodobenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 25A for the product of Example 1B (0.176 g, 60%). MS (ESI-) m/z 557 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.47 (s, 2H), 7.07 (t, *J*=7.72 Hz, 1H), 7.17 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 3H), 7.55 (m, 2H), 7.66 (m, 2H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.78, 1.84 Hz, 1H), 15.79 (s, 1H).

Example 26

1-[(3,5-dimethyl-4-isoxazolyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 26A

1-[(3,5-dimethyl-4-isoxazolyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-chloromethyl-3,5-dimethylisoxazole for n-butyl bromide (0.199 g, 60%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.20 (s, 3H), 2.45 (s, 3H), 5.10 (s, 2H), 7.40 (dd, *J*=7.72, 4.78 Hz, 1H), 8.40 (dd, *J*=7.72, 1.84 Hz, 1H), 8.80 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 26B

1-[(3,5-dimethyl-4-isoxazolyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 26A for the product of Example 1B (0.187 g, 63%). MS (DCI/NH_3) m/z 452 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 2.20 (s, 3H), 2.38 (s, 3H), 5.44 (s, 2H), 7.51 (dd, *J*=7.90, 4.60 Hz, 1H), 7.55 (t, *J*=7.17 Hz, 1H), 7.64 (d, *J*=7.72 Hz, 1H), 7.77 (t, *J*=7.17 Hz, 1H), 7.92 (d, *J*=7.72 Hz, 1H), 8.58 (dd, *J*=7.90, 1.66 Hz, 1H), 8.88 (dd, *J*=4.60, 1.66 Hz, 1H), 13.95 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 2.17 (s, 3H), 2.29 (s, 3H), 5.26 (s, 2H), 7.17 (dd, *J*=7.73, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (t, *J*=7.72 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.39 (dd, *J*=7.72, 1.84 Hz, 1H), 8.53 (dd, *J*=4.78, 1.84 Hz, 1H), 15.78 (s, 1H).

Example 27

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[2-(3-thienyl)ethyl]-1,8-naphthyridin-2(1H)-one

Example 27A

1-[2-(3-thienyl)ethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-(2-bromoethyl)thiophene for n-butyl bromide (0.156 g, 46%). ^1H NMR (300 MHz, DMSO-d_6) δ 2.98 (t, 2H), 4.36 (t, 2H), 7.07 (d, *J*=5.15 Hz, 1H), 7.31 (m, 1H), 7.39 (dd, *J*=7.72, 5.15 Hz, 1H), 7.49 (m, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.78 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 27B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[2-(3-thienyl)ethyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 27A for the product of Example 1B (0.123 g, 48%). MS (ESI-) m/z 451 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 2.90 (t, *J*=7.90 Hz, 2H), 4.51 (t, *J*=7.90 Hz, 2H), 7.10 (d, *J*=4.78 Hz, 1H), 7.16 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 3H), 7.49 (dd, *J*=4.78, 2.94 Hz, 1H), 7.56 (m, 1H), 7.68 (d, *J*=7.72 Hz, 1H), 8.39 (dd, *J*=7.72, 1.84 Hz, 1H), 8.55 (dd, *J*=4.78, 1.84 Hz, 1H), 15.89 (s, 1H).

Example 28

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-pyridinylmethyl)-1,8-naphthyridin-2(1H)-one

Example 28A

1-(4-pyridinylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-(chloromethyl)pyridine for n-butyl bromide (0.089 g, 29%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.37 (s, 2H), 7.41 (m, 3H), 8.45 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (m, 2H), 8.69 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 28B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-pyridinylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 28A for the product of Example 1B (0.034 g, 19%). MS (DCI/NH_3) m/z 434 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.83 (s, 2H), 7.52 (m, 2H), 7.60 (d, *J*=7.72 Hz, 1H), 7.69 (d, *J*=6.25 Hz, 2H), 7.73 (m, 1H), 7.91 (d, *J*=6.99 Hz, 1H), 8.62 (dd, *J*=7.72, 1.84 Hz, 1H), 8.68 (d, *J*=6.25 Hz, 2H), 8.75 (dd, *J*=4.78, 1.84 Hz, 1H), 13.98 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.56 (s, 2H), 7.22 (m, 3H), 7.33 (m, 2H), 7.59 (m, 1H), 7.71 (m, 1H), 8.45 (m, 3H), 8.50 (dd, *J*=4.78, 1.83 Hz, 1H), 15.54 (s, 1H).

Example 29

1-(4-bromobenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 29A

1-(4-bromobenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-bromobenzyl bromide for n-butyl bromide (1.460 g, 72%). MS (DCI) m/z 333 $(M+H)^+$.

Example 29B

1-(4-bromobenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 29A for the product of Example 1B (0.060 g, 59%). MS (ESI-) m/z 509 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.47 (s, 2H), 7.16 (dd, *J*=7.72, 4.78 Hz, 1H), 7.22 (d, *J*=8.46 Hz, 2H), 7.27 (t, *J*=7.72 Hz, 2H), 7.44 (d, *J*=8.46 Hz, 2H), 7.56 (td, *J*=7.72, 1.47 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.48 (dd, *J*=4.78, 1.84 Hz, 1H), 15.80 (s, 1H).

Example 30

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-neopentyl-1,8-naphthyridin-

2(1H)-one

Example 30A

ethyl 2-(neopentylamino)nicotinate

The title compound was prepared according to the procedure of Example 3A substituting 2,2-dimethylpropylamine for 2-ethylbutylamine (0.407 g, 57 %). MS (ESI+) 237 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 1.02 (s, 9H), 1.38 (t, *J*=7.17 Hz, 3H), 3.36 (d, *J*=5.52 Hz, 2H), 4.33 (q, *J*=7.35 Hz, 2H), 6.48 (dd, *J*=7.91, 4.60 Hz, 1H), 8.12 (dd, *J*=7.72, 2.21 Hz, 1H), 8.16 (s, 1H), 8.26 (dd, *J*=4.78, 2.21 Hz, 1H).

Example 30B

1-neopentyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 30A for the product of Example 3A (0.182 g, 89 %). ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (s, 9H), 4.28 (s, 2H), 7.25 (dd, *J*=6.99, 4.04 Hz, 1H), 8.41 (dd, *J*=7.91, 2.02 Hz, 1H), 8.69 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 30C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-neopentyl-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 30B for the product of Example 1B (0.070 g, 22 %). MS (ESI+) m/z 413 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 0.96 (s, 9H), 4.52 (s, 2H), 7.49 (dd, *J*=8.09, 4.41 Hz, 1H), 7.56 (t, *J*=7.54 Hz, 1H), 7.68 (d, *J*=8.09 Hz, 1H), 7.78 (m, 1H), 7.94 (d, *J*=6.99 Hz, 1H), 8.57 (dd, *J*=8.09, 1.84 Hz, 1H), 8.85 (dd, *J*=4.41, 1.84 Hz, 1H), 14.11 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI+) m/z 413 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 0.91 (s, 9H), 4.34 (s, 2H), 7.11 (dd, *J*=7.72, 4.78 Hz, 1H), 7.27 (m, 2H), 7.55 (m, 1H), 7.66 (m, 1H), 8.36 (dd, *J*=7.54, 2.02 Hz, 1H), 8.48 (dd, *J*=4.60, 2.02 Hz, 1H), 15.95 (s, 1H).

Example 31

1-{[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 31A

ethyl 2-({[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}amino)nicotinate

The title compound was prepared according to the procedure of Example 3A substituting (-)-cis-myrtanylamine for 2-ethylbutylamine (0.604 g, 40%). MS (ESI+) m/z 303 $(M+H)^+$.

Example 31B

1-{[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 31A for the product of Example 3A (0.570 g, 95%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.79 (d, *J*=9.56 Hz, 1H), 1.14 (s, 3H), 1.22 (s, 3H), 1.62 (m, 1H), 1.87 (m, 5H), 2.26 (m, 1H), 2.53 (m, 1H), 4.04 (dd, *J*=13.05, 6.07 Hz, 1H), 4.28 (dd, *J*=13.24, 9.19 Hz, 1H), 7.37 (dd, *J*=7.72, 4.78 Hz, 1H), 8.38 (dd, *J*=7.72, 1.84 Hz, 1H), 8.76 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 31C

1-{[(1S,2R,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]methyl}-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 31B for the product of Example 1B (0.050 g, 21%). MS (ESI-) m/z 477 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.78 (d, *J*=9.56 Hz, 1H), 1.15 (m, 3H), 1.30 (s, 3H), 1.80 (m, 6H), 2.24 (m, 1H), 2.54 (m, 1H), 4.37 (m, 2H), 7.12 (dd, *J*=7.54, 4.60 Hz, 1H), 7.27 (m, 2H), 7.55 (m, 1H), 7.67 (dd, *J*=7.72, 1.47 Hz, 1H), 8.36 (dd, *J*=7.54, 2.02 Hz, 1H), 8.50 (dd, *J*=4.60, 2.02 Hz, 1H), 15.95 (s, 1H).

Example 32

3-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzonitrile

Example 32A

3-[(2,4-dioxo-2H-pyrido[2,3-d][1,3]oxazin-1(4H)-yl)methyl]benzonitrile

The title compound was prepared according to the procedure of Example 1B substituting 3-cyanobenzyl bromide for n-butyl bromide (0.363 g, 71%). MS (DCI) m/z 280 $(M+H)^+$.

Example 32B

3-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzonitrile

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 32A for the product of Example 1B (0.024 g, 22%). MS (ESI-) m/z 456 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.54 (s, 2H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.48 (t, *J*=7.72 Hz, 1H), 7.56 (td, *J*=7.91, 1.47 Hz, 2H), 7.68 (m, 3H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.60, 2.02 Hz, 1H), 15.77 (s, 1H).

Example 33

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-pyridinylmethyl)-1,8-naphthyridin-2(1H)-one

Example 33A

1-(3-pyridinylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-(bromomethyl)pyridine for n-butyl bromide (0.153 g, 49%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.38 (s, 2H), 7.34 (dd, *J*=7.72, 4.78 Hz, 1H), 7.40 (dd, *J*=7.72, 4.78 Hz, 1H), 7.82 (m, 1H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.47 (dd, *J*=4.78, 1.10 Hz, 1H), 8.66 (d, *J*=1.84 Hz, 1H), 8.74 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 33B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-pyridinylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 33A for the product of Example 1B (0.098 g, 41%). MS (DCI/NH_3) m/z 434 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.72 (s, 2H), 7.41 (dd, *J*=7.72, 4.78 Hz, 1H), 7.50 (m, 2H), 7.61 (d, *J*=8.09 Hz, 1H), 7.74 (m, 1H), 7.84 (d, *J*=7.72 Hz, 1H), 7.89 (d, *J*=8.09 Hz, 1H), 8.50 (d, *J*=4.04 Hz, 1H), 8.58 (dd, *J*=7.73, 1.84 Hz, 1H), 8.67 (s, 1H), 8.80 (dd, *J*=4.78, 1.84 Hz, 1H), 14.15 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.53 (s, 2H), 7.18 (dd, *J*=7.72, 4.41 Hz, 1H), 7.29 (m, 3H), 7.56 (m, 1H), 7.65 (m, 2H), 8.40 (m, 2H), 8.51 (dd, *J*=4.60, 2.02 Hz, 1H), 8.57 (d, *J*=1.47 Hz, 1H), 15.78 (s, 1H).

Example 34

1-(1-adamantylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 34A

2-[(1-adamantylmethyl)amino]nicotinic acid

The title compound was prepared according to the procedure of Example 3A substituting 2-chloronicotinic acid for ethyl 2-chloronicotinate and 1-adamantanemethylamine for 2-ethylbutylamine (0.185 g, 79 %). MS (ESI+) m/z 287.1 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.74 (m, 12H), 2.00 (s, 3H), 3.31 (m, 2H), 6.60 (dd, *J*=7.35, 5.52 Hz, 1H), 7.96 (dd, *J*=5.33, 2.02 Hz, 1H), 8.26 (dd, *J*=7.35, 1.84 Hz, 1H).

Example 34B

1-(1-adamantylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 34A for the product of Example 3A (0.025 g, 20 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.74 (m, 12H), 2.04 (s, 3H), 3.65 (d, *J*=5.88 Hz, 2H), 6.91 (dd, *J*=7.72, 5.52 Hz, 1H), 8.51 (d, *J*=4.78 Hz, 1H), 8.77 (d, *J*=7.72 Hz, 1H).

Example 34C

1-(1-adamantylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-

naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 34B for the product of Example 1B (0.018 g, 47 %). MS (ESI+) m/z 491.1 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.59 (s, 12H), 1.90 (m, 3H), 4.41 (br s, 2H), 7.48 (m, 1H), 7.56 (t, *J*=7.54 Hz, 1H), 7.69 (m, 1H), 7.77 (m, 1H), 7.94 (d, *J*=7.72 Hz, 1H), 8.56 (dd, *J*=8.09, 1.84 Hz, 1H), 8.85 (dd, *J*=4.60, 1.65 Hz, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI+) m/z 491.1 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.56 (m, 12H), 1.87 (s, 3H), 4.21 (br s, 2H), 7.10 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.55 (m, 1H), 7.66 (dd, *J*=7.72, 1.47 Hz, 1H), 8.35 (dd, *J*=7.72, 1.84 Hz, 1H), 8.48 (dd, *J*=4.60, 2.02 Hz, 1H), 15.97 (br s, 1H).

Example 35

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[3-(trifluoromethyl)benzyl]-1,8-naphthyridin-2(1H)-one

Example 35A

1-[3-(trifluoromethyl)benzyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-(trifluoromethyl)benzyl bromide for n-butyl bromide (0.250 g, 42%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.43 (s, 2H), 7.40 (dd, *J*=7.72, 4.78 Hz, 1H), 7.55 (m, 1H), 7.64 (m, 1H), 7.73 (d, *J*=7.72 Hz, 1H), 7.81 (s, 1H), 8.43 (dd, *J*=7.72, 1.84 Hz, 1H), 8.72 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 35B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[3-(trifluoromethyl)benzyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 35A for the product of Example 1B (0.22 g, 57 %). MS (ESI-) m/z 499 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.77 (s, 2H), 7.54 (m, 6H), 7.66 (d, *J*=7.72 Hz, 1H), 7.76 (m, 2H), 7.92 (d, *J*=8.09 Hz, 1H), 8.61 (dd, *J*=8.09, 1.84 Hz, 1H), 8.83 (dd, *J*=4.41, 1.84 Hz, 1H), 13.91 (br s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 499 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.58 (s, 2H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.54 (m, 4H), 7.66 (m, 2H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.60, 2.02 Hz, 1H), 15.78 (m, 1H).

Example 36

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2-methyl-1,3-thiazol-5-yl)methyl]-1,8-naphthyridin-2(1H)-one

Example 36A

1-[(2-methyl-1,3-thiazol-5-yl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-methyl-5-chloromethylthiazole for n-butyl bromide (0.300 g, 54%).

Example 36B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2-methyl-1,3-thiazol-5-yl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 36A for the product of Example 1B (0.123 g, 25%). MS (ESI-) m/z 452 $(M-H)^-$; ^1H NMR (300 MHz, DMSO-d_6) δ 2.54 (s, 3H), 5.76 (s, 1H), 7.53 (m, 1H), 7.52 (d, *J*=7.72 Hz, 1H), 7.65 (m, 2H), 7.76 (t, *J*=7.72 Hz, 1H), 7.91 (d, *J*=7.72 Hz, 1H), 8.57 (d, *J*=7.72 Hz, 1H), 8.90 (d, *J*=4.04 Hz, 1H), 13.92 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D.

Example 37

1-(2-cyclohexylethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 37A

1-(2-cyclohexylethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 1-bromo-2-cyclohexylethane for n-butyl bromide (0.196 g, 39%).

Example 37B

1-(2-cyclohexylethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 37A for the product of Example 1B (0.030 g, 18 % after column purification). MS (ESI-) m/z 451 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 451 $(M-H)^-$; ^1H NMR (300 MHz, DMSO-d_6/TFA) δ 0.78 (m, 2H), 0.98 (m, 3H), 1.18 (m, 1H), 1.40 (m, 5H), 1.59 (d, *J*=12.50 Hz, 2H), 4.33 (m, 2H), 7.23 (m, 3H), 7.47 (t, *J*=7.54 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.43 (m, 1H), 8.57 (dd, *J*=4.78, 1.47 Hz, 1H).

Example 38

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-methoxybenzyl)-1,8-naphthyridin-2(1H)-one

Example 38A

1-(4-methoxybenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-methoxybenzyl chloride for n-butyl bromide (0.364 g, 70%). MS (DCI) m/z

285 $(M+H)^+$.

Example 38B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-methoxybenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 38A for the product of Example 1B (0.098 g, 51%). MS (ESI-) m/z 461 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.68 (s, 3H), 5.45 (s, 2H), 6.80 (dt, *J*=8.82, 2.21 Hz, 2H), 7.15 (dd, *J*=7.72, 4.78 Hz, 1H), 7.26 (m, 4H), 7.55 (td, *J*=7.72, 1.47 Hz, 1H), 7.67 (dd, *J*=7.91, 1.65 Hz, 1H), 8.39 (dd, *J*=7.72, 2.21 Hz, 1H), 8.50 (dd, *J*=4.78, 1.84 Hz, 1H), 15.86 (s, 1H).

Example 39

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-methylbenzyl)-1,8-naphthyridin-2(1H)-one

Example 39A

1-(2-methylbenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-methylbenzyl bromide for n-butyl bromide (0.353 g, 72%). MS (DCI) m/z 269 $(M+H)^+$.

Example 39B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-methylbenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 39A for the product of Example 1B (0.165 g, 62%). MS (ESI-) m/z 445 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.44 (s, 3H), 5.45 (s, 2H), 6.59 (d, *J*=7.35 Hz, 1H), 6.96 (t, *J*=7.17 Hz, 1H), 7.06 (t, *J*=6.80 Hz, 1H), 7.16 (m, 2H), 7.29 (t, *J*=7.54 Hz, 2H), 7.56 (td, *J*=7.72, 1.47 Hz, 1H), 7.66 (d, *J*=7.72 Hz, 1H), 8.43 (d, *J*=6.25 Hz, 2H), 15.84 (s, 1H).

Example 40

1-(cyclopropylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 40A

1-(cyclopropylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting (bromomethyl)cyclopropane for n-butyl bromide (0.278 g, 70%). MS (APCI+) m/z 219 (M+H). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.46 (m, 4H), 1.27 (m, 1H), 4.04 (d,

J=6.99 Hz, 2H), 7.39 (dd, J=7.91, 4.96 Hz, 1H), 8.40 (dd, J=7.72, 1.84 Hz, 1H), 8.78 (dd, J=4.78, 1.84 Hz, 1H).

Example 40B

1-(cyclopropylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 40A for the product of Example 1B (0.06 g, 20 % after column purification). MS (ESI-) m/z 395 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 395 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.40 (m, 4H), 1.32 (m, 1H), 4.19 (d, J=6.99 Hz, 2H), 7.14 (dd, J=7.54, 4.60 Hz, 1H), 7.28 (m, 2H), 7.55 (t, J=7.35 Hz, 1H), 7.67 (dd, J=7.72, 1.10 Hz, 1H), 8.38 (dd, J=7.72, 1.84 Hz, 1H), 8.52 (dd, J=4.60, 2.02 Hz, 1H), 15.93 (s, 1H).

Example 41

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(1,3-thiazol-4-ylmethyl)-1,8-naphthyridin-2(1H)-one

Example 41A

1-(1,3-thiazol-4-ylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-(chloromethyl)thiazole for n-butyl bromide (0.049 g, 15%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.48 (s, 2H), 7.40 (dd, J=7.72, 4.78 Hz, 1H), 7.66 (s, 1H), 8.45 (dd, J=7.72, 1.84 Hz, 1H), 8.72 (dd, J=4.78, 1.84 Hz, 1H), 9.06 (d, J=2.21 Hz, 1H).

Example 41B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(1,3-thiazol-4-ylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 41A for the product of Example 1B (0.046 g, 59%). MS (ESI-) m/z 438 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.65 (s, 2H), 7.04 (d, J=2.21 Hz, 1H), 7.16 (dd, J=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (m, 1H), 7.66 (d, J=7.35 Hz, 1H), 8.42 (dd, J=7.72, 2.21 Hz, 1H), 8.46 (dd, J=4.78, 2.20 Hz, 1H), 8.98 (d, J=1.84 Hz, 1H), 15.85 (s, 1H).

Example 42

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-phenyl-2-thienyl)methyl]-1,8-naphthyridin-2(1H)-one

The product of Example 4B (100 mg, 0.193 mmol), phenylboronic acid (49 mg, 0.387 mmol), 2M aqueous Na_2CO_3 (0.45 mL), absolute ethanol (0.5 mL), and

tetrakis(triphenylphosphine)palladium (14 mg, 0.012 mmol) in N_2-sparged DMF (2 mL) was heated to reflux for 2.5 hours, cooled to 0 °C, diluted with H_2O (15 mL), adjusted to pH 3 with 1N HCl, and extracted with ethyl acetate (3 x 25 mL). The combined extracts were washed with saturated NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash column chromatography on silica gel with 3% ethyl acetate/dichloromethane to give the title compound (0.039 g, 40%). MS (ESI-) m/z 513 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 5.64 (s, 2H), 7.12 (d, *J*=3.68 Hz, 1H), 7.20 (dd, *J*=7.72, 4.78 Hz, 1H), 7.31 (m, 6H), 7.57 (m, 3H), 7.68 (d, *J*=7.72 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.60 (dd, *J*=4.78, 1.84 Hz, 1H), 15.80 (s, 1H).

Example 43

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-methyl-3-pentenyl)-1,8-naphthyridin-2(1H)-one

Example 43A

1-(4-methyl-3-pentenyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 5-bromo-2-methyl-2-pentene for n-butyl bromide (0.157 g, 35%). MS (DCI+) m/z 247 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 1.59 (s, 3H), 1.66 (s, 3H), 2.35 (m, 2H), 4.09 (m, 2H), 5.18 (t, *J*=7.54 Hz, 1H), 7.39 (dd, *J*=7.72, 5.15 Hz, 1H), 8.40 (dd, *J*=7.72, 1.84 Hz, 1H), 8.79 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 43B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(4-methyl-3-pentenyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 43A for the product of Example 1B (0.030 g, 20 % after recrystallization). MS (ESI-) m/z 423 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 423 $(M-H)^-$; ^1H NMR (300 MHz, DMSO-d_6) δ 1.63 (s, 3H), 1.67 (s, 3H), 2.26 (m, 2H), 4.23 (m, 2H), 5.21 (m, 1H), 7.14 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.55 (t, *J*=7.35 Hz, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.37 (dd, *J*=7.72, 2.21 Hz, 1H), 8.53 (dd, *J*=4.60, 2.02 Hz, 1H), 15.92 (s, 1H).

Example 44

4-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzonitrile

Example 44A

4-[(2,4-dioxo-2H-pyrido[2,3-d][1,3]oxazin-1(4H)-yl)methyl]benzonitrile

The title compound was prepared according to the procedure of Example 1B substituting 4-cyanobenzyl bromide for n-butyl bromide (1.02 g, 60%). MS (DCI) m/z 280

$(M+H)^+$.

Example 44B

4-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzonitrile

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 44A for the product of Example 1B (0.197 g, 60%). MS (ESI-) m/z 456 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.58 (s, 2H), 7.18 (dd, *J*=7.54, 4.60 Hz, 1H), 7.29 (td, *J*=8.46, 1.84 Hz, 2H), 7.41 (d, *J*=8.46 Hz, 2H), 7.56 (td, *J*=7.81, 1.65 Hz, 1H), 7.67 (dd, *J*=7.91, 1.29 Hz, 1H), 7.72 (d, *J*=8.46 Hz, 2H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.46 (dd, *J*=4.60, 2.02 Hz, 1H), 15.77 (s, 1H).

Example 45

1-[2-(1-cyclohexen-1-yl)ethyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 45A

ethyl 2-{[2-(1-cyclohexen-1-yl)ethyl]amino}nicotinate

The title compound was prepared according to the procedure of Example 3A substituting 2-(1-cyclohexenyl)ethylamine for 2-ethylbutylamine (2.2 g, 80%). MS (DCI) m/z 275 $(M+H)^+$.

Example 45B

1-[2-(1-cyclohexen-1-yl)ethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 45A for the product of Example 3A (0.493 g, 91%). MS (DCI) m/z 290 $(M+NH_4)^+$.

Example 45C

1-[2-(1-cyclohexen-1-yl)ethyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 45B for the product of Example 1B (0.048 g, 14%). MS (ESI-) m/z 449 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.53 (m, 4H), 1.90 (m, 2H), 2.05 (m, 2H), 2.18 (t, *J*=7.54 Hz, 2H), 4.36 (m, 2H), 5.38 (s, 1H), 7.13 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.55 (td, *J*=7.72, 1.47 Hz, 1H), 7.66 (dd, *J*=7.72, 1.47 Hz, 1H), 8.37 (dd, *J*=7.54, 2.02 Hz, 1H), 8.52 (dd, *J*=4.60, 2.02 Hz, 1H), 15.91 (s, 1H).

Example 46

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2-methyl-1,3-thiazol-4-yl)methyl]-1,8-naphthyridin-2(1H)-one

Example 46A

1-[(2-methyl-1,3-thiazol-4-yl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-chloromethyl-2-methylthiazole for n-butyl bromide (0.087 g, 26%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.63 (s, 3H), 5.37 (d, J=1.47 Hz, 2H), 7.39 (s, 1H), 7.40 (dd, J=7.72, 4.78 Hz, 1H), 8.44 (dd, J=7.72, 1.84 Hz, 1H), 8.72 (dd, J=4.78, 1.84 Hz, 1H).

Example 46B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(2-methyl-1,3-thiazol-4-yl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 46A for the product of Example 1B (0.078 g, 56%). MS (DCI/NH_3) m/z 454 $(M+H)^+$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.61 (s, 3H), 5.55 (s, 2H), 6.74 (s, 1H), 7.16 (dd, J=7.73, 4.78 Hz, 1H), 7.29 (m, 2H), 7.55 (m, 1H), 7.67 (d, J=7.72 Hz, 1H), 8.41 (dd, J=7.72, 1.84 Hz, 1H), 8.47 (dd, J=4.78, 2.21 Hz, 1H), 15.85 (s, 1H).

Example 47

2-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzonitrile

Example 47A

2-[(2,4-dioxo-2H-pyrido[2,3-d][1,3]oxazin-1(4H)-yl)methyl]benzonitrile

The title compound was prepared according to the procedure of Example 1B substituting 2-cyanobenzyl bromide for n-butyl bromide (0.332 g, 65%). MS (DCI) m/z 280 $(M+H)^+$.

Example 47B

2-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzonitrile

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 47A for the product of Example 1B (0.183 g, 66%). MS (ESI-) m/z 456 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.68 (s, 2H), 7.00 (d, J=8.09 Hz, 1H), 7.19 (dd, J=7.35, 4.78 Hz, 1H), 7.30 (t, J=8.09 Hz, 2H), 7.39 (t, J=7.54 Hz, 1H), 7.56 (t, J=7.85 Hz, 2H), 7.67 (d, J=7.72 Hz, 1H), 7.84 (d, J=7.72 Hz, 1H), 8.44 (m, 2H), 15.75 (s, 1H).

Example 48

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-methyl-3-isoxazolyl)methyl]-1,8-naphthyridin-2(1H)-one

Example 48A

1-[(5-methyl-3-isoxazolyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-chloromethyl-5-methylisoxazole for n-butyl bromide (0.047 g, 15%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.34 (s, 3H), 5.35 (s, 2H), 6.26 (d, *J*=1.10 Hz, 1H), 7.42 (dd, *J*=7.72, 4.78 Hz, 1H), 8.44 (dd, *J*=7.72, 1.84 Hz, 1H), 8.75 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 48B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(5-methyl-3-isoxazolyl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 48A for the product of Example 1B (0.051 g, 67%). MS (ESI-) m/z 436 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.29 (s, 3H), 5.50 (s, 2H), 5.94 (s, 1H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (t, *J*=8.09 Hz, 1H), 7.67 (d, *J*=8.09 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.78, 2.21 Hz, 1H), 15.76 (s, 1H).

Example 49

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(1-naphthylmethyl)-1,8-naphthyridin-2(1H)-one

Example 49A

1-(2-naphthylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 1-(bromomethyl)naphthalene for n-butyl bromide (0.391 g, 71%). MS (DCI) m/z 305 $(M+H)^+$.

Example 49B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(1-naphthylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 49A for the product of Example 1B (0.087 g, 60%). MS (ESI-) m/z 481 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.88 (s, 2H), 7.45 (m, 2H), 7.54 (t, *J*=7.72 Hz, 3H), 7.65 (d, *J*=7.72 Hz, 1H), 7.75 (m, 2H), 7.81 (dd, *J*=6.07, 3.49 Hz, 1H), 7.86 (d, *J*=8.46 Hz, 2H), 7.93 (d, *J*=7.35 Hz, 1H), 8.63 (dd, *J*=7.72, 1.84 Hz, 1H), 8.83 (dd, *J*=4.78, 1.84 Hz, 1H), 14.04 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.69 (s, 2H), 7.16 (dd, *J*=7.54, 4.60 Hz, 1H), 7.29 (t, *J*=7.72 Hz, 2H), 7.43 (m, 2H), 7.49 (dd, *J*=8.64, 1.65 Hz, 1H), 7.56 (td, *J*=7.72, 1.47 Hz, 1H), 7.67 (d, *J*=7.35 Hz, 2H), 7.83 (m, 3H), 8.42 (dd, *J*=7.54, 2.02 Hz, 1H), 8.48 (dd, *J*=4.60, 2.02 Hz, 1H), 15.86 (s, 1H).

Example 50

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-pyridinylmethyl)-1,8-naphthyridin-2(1H)-one

Example 50A

1-(2-pyridinylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-(bromomethyl)pyridine for n-butyl bromide (0.060 g, 19%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.45 (s, 2H), 7.26 (m, 1H), 7.39 (dd, *J*=7.72, 4.78 Hz, 1H), 7.45 (d, *J*=8.09 Hz, 1H), 7.73 (m, 1H), 8.46 (dd, *J*=7.72, 1.84 Hz, 1H), 8.47 (m, 1H), 8.68 (dd, *J*=4.78, 1.47 Hz, 1H).

Example 50B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-pyridinylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 50A for the product of Example 1B (0.072 g, 72%). MS (ESI-) m/z 432 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.62 (s, 2H), 6.97 (d, *J*=8.09 Hz, 1H), 7.18 (m, 2H), 7.31 (m, 2H), 7.62 (m, 3H), 8.44 (d, *J*=6.62 Hz, 3H), 15.71 (s, 1H).

Example 51

1-(4-tert-butylbenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 51A

1-(4-tert-butylbenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-(tert-butyl)benzyl bromide for n-butyl bromide (0.410 g, 72%). MS (DCI) m/z 311 $(M+H)^+$.

Example 51B

1-(4-tert-butylbenzyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 51A for the product of Example 1B (0.109 g, 70%). MS (ESI-) m/z 487 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.23 (s, 9H), 5.49 (s, 2H), 7.16 (m, 3H), 7.28 (m, 4H), 7.55 (td, *J*=7.91, 1.47 Hz, 1H), 7.66 (d, *J*=6.25 Hz, 1H), 8.40 (dd, *J*=7.72, 2.21 Hz, 1H), 8.49 (dd, *J*=4.60, 2.02 Hz, 1H), 15.84 (s, 1H).

Example 52

ethyl [3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-

1(2H)-yl]acetate

Example 52A

ethyl (2,4-dioxo-2H-pyrido[2,3-d][1,3]oxazin-1(4H)-yl)acetate

The title compound was prepared according to the procedure of Example 1B substituting ethyl bromoacetate for n-butyl bromide (0.174 g, 43%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.21 (t, J=7.17 Hz, 3H), 4.18 (q, J=7.11 Hz, 2H), 4.92 (s, 2H), 7.45 (dd, J=7.72, 4.78 Hz, 1H), 8.47 (dd, J=7.91, 1.65 Hz, 1H), 8.77 (dd, J=4.78, 1.84 Hz, 1H).

Example 52B

ethyl [3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]acetate

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 52A for the product of Example 1B (0.200 g, 52 %). MS (ESI-) m/z 427 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6/CF_3COOD) δ 1.26 (t, J=6.99 Hz, 3H), 4.22 (q, J=7.11 Hz, 2H), 5.34 (s, 2H), 7.44 (dd, J=7.91, 4.60 Hz, 1H), 7.54 (m, 2H), 7.74 (m, 1H), 7.96 (m, 1H), 8.63 (dd, J=8.09, 1.84 Hz, 1H), 8.79 (dd, J=4.78, 1.84 Hz, 1H).

Example 53

[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]acetic acid

To a suspension of the product of Example 52B in 1:1 THF:methanol (6 mL) was added 0.5 N aqueous lithium hydroxide (6 mL). The mixture was stirred at room temperature for 2 hours, adjusted to pH 3 with 1.0 N HCl, and filtered. The filter cake was washed with water and dried to give the title compound (0.133 g, 86%). MS (ESI-) m/z 399 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.16 (s, 2H), 7.54 (m, 2H), 7.67 (d, J=7.72 Hz, 1H), 7.77 (t, J=7.72 Hz, 1H), 7.92 (d, J=7.72 Hz, 1H), 8.60 (dd, J=8.09, 1.84 Hz, 1H), 8.84 (dd, J=4.60, 1.65 Hz, 1H), 13.11 (br s, 1H), 13.79 (br s, 1H).

Example 54

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-phenoxybenzyl)-1,8-naphthyridin-2(1H)-one

Example 54A

1-(3-phenoxybenzyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 3-phenoxybenzyl chloride for n-butyl bromide (0.190 g, 31%). MS (DCI) m/z 347 $(M+H)^+$.

Example 54B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-phenoxybenzyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 54A for the product of Example 1B (0.063 g, 52%). MS (ESI-) m/z 523 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.51 (s, 2H), 6.77 (dd, *J*=8.09, 1.47 Hz, 1H), 6.91 (s, 1H), 6.99 (t, *J*=8.46 Hz, 2H), 7.10 (t, *J*=7.35 Hz, 1H), 7.19 (m, 1H), 7.31 (m, 6H), 7.57 (t, *J*=7.72 Hz, 1H), 7.68 (d, *J*=7.72 Hz, 1H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.48 (d, *J*=2.94 Hz, 1H), 15.74 (s, 1H).

Example 55

1-allyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 55A

1-allyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting allyl bromide for n-butyl bromide (5.12 g, 82%). MS (DCI/NH_3) m/z 205 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.75 (m, 2H), 5.14 (dd, *J*=10.66, 1.47 Hz, 1H), 5.27 (dd, *J*=17.28, 1.47 Hz, 1H), 5.92 (m, 1H), 7.39 (dd, *J*=7.72, 4.78 Hz, 1H), 8.40 (dd, *J*=7.91, 2.02 Hz, 1H), 8.75 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 55B

1-allyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 55A for the product of Example 1B (1.4g, 34.5%). MS (DCI/NH_3) m/z 383 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.03 (m, 1H), 5.11-5.15 (m, 3H), 5.93-6.07 (m, 1H), 7.45-7.60 (m, 2H), 7.65-7.72 (m, *J*=8.46 Hz, 1H), 7.73-7.80 (t, *J*=7.72 Hz, 1H), 7.92 (d, *J*=7.35 Hz, 1H), 8.58 (dd, *J*=8.09, 1.84 Hz, 1H), 8.85 (dd, *J*=4.60, 1.65 Hz, 1H).

Example 56

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-naphthylmethyl)-1,8-naphthyridin-2(1H)-one

Example 56A

1-(2-naphthylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-(bromomethyl)naphthalene for n-butyl bromide (0.417 g, 75%). MS (DCI) m/z 305 $(M+H)^+$.

Example 56B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-naphthylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 56A for the product of Example 1B (0.022 g, 42%). MS (ESI-) m/z 481 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.18 (s, 2H), 6.83 (d, *J*=6.62 Hz, 1H), 7.28 (m, 1H), 7.53 (t, *J*=7.54 Hz, 2H), 7.68 (m, 4H), 7.81 (d, *J*=8.09 Hz, 1H), 7.92 (d, *J*=7.35 Hz, 1H), 8.00 (d, *J*=8.09 Hz, 1H), 8.32 (d, *J*=8.46 Hz, 1H), 8.66 (dd, *J*=8.09, 1.84 Hz, 1H), 8.74 (dd, *J*=4.78, 1.84 Hz, 1H), 14.04 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.00 (s, 2H), 6.76 (d, *J*=6.25 Hz, 1H), 7.18 (dd, *J*=7.54, 4.96 Hz, 1H), 7.30 (m, 3H), 7.63 (m, 4H), 7.75 (d, *J*=8.09 Hz, 1H), 7.97 (d, *J*=6.99 Hz, 1H), 8.31 (d, *J*=8.46 Hz, 1H), 8.40 (d, *J*=3.68 Hz, 1H), 8.47 (dd, *J*=7.72, 1.84 Hz, 1H), 15.78 (s, 1H).

Example 57

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(1R)-1-phenylethyl]-1,8-naphthyridin-2(1H)-one

Example 57A

ethyl 2-{[(1R)-1-phenylethyl]amino}nicotinate

The title compound was prepared according to the procedure of Example 3A substituting (R)-(+)-α-methylbenzylamine for 2-ethylbutylamine (2.23 g, 82%). MS (DCI) m/z 271 $(M+H)^+$.

Example 57B

1-[(1R)-1-phenylethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 57A for the product of Example 3A (0.250 g, 62%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.86 (d, *J*=6.99 Hz, 3H), 6.65 (q, *J*=6.99 Hz, 1H), 7.27 (m, 3H), 7.40 (m, 3H), 8.43 (dd, *J*=7.72, 1.84 Hz, 1H), 8.73 (dd, *J*=4.96, 2.02 Hz, 1H).

Example 57C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(1R)-1-phenylethyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 57B for the product of Example 1B (0.080 g, 36%). MS (ESI-) m/z 445 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.90 (d, *J*=7.35 Hz, 3H), 6.87 (m, 1H), 7.12 (m, 2H), 7.25 (m, 6H), 7.55 (m, 1H), 7.65 (d, *J*=7.72 Hz, 1H), 8.40 (d, *J*=6.25 Hz, 2H), 15.92 (s, 1H).

Example 58

1-[(5-tert-butyl-2-thienyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-

1,8-naphthyridin-2(1H)-one

Example 58A

1-[(5-tert-butyl-2-thienyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-bromomethyl-5-tert-butylthiophene for n-butyl bromide (0.098 g, 25%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.28 (s, 9H), 5.39 (s, 2H), 6.71 (d, *J*=3.68 Hz, 1H), 7.00 (d, *J*=3.68 Hz, 1H), 7.42 (dd, *J*=7.72, 4.78 Hz, 1H), 8.40 (dd, *J*=7.72, 1.47 Hz, 1H), 8.83 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 58B

1-[(5-tert-butyl-2-thienyl)methyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 58A for the product of Example 1B (0.082 g, 54%). MS (ESI-) m/z 493 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.25 (s, 9H), 5.55 (s, 2H), 6.63 (d, *J*=3.31 Hz, 1H), 6.89 (d, *J*=3.31 Hz, 1H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.28 (m, 2H), 7.56 (m, 1H), 7.67 (d, *J*=7.72 Hz, 1H), 8.39 (dd, *J*=7.72, 1.84 Hz, 1H), 8.57 (dd, *J*=4.78, 1.84 Hz, 1H), 15.83 (s, 1H).

Example 59

1-(1,1'-biphenyl-4-ylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 59A

1-(1,1'-biphenyl-4-ylmethyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 4-phenylbenzyl chloride for n-butyl bromide (0.119 g, 20%). MS (DCI) m/z 331 $(M+H)^+$.

Example 59B

1-(1,1'-biphenyl-4-ylmethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 59A for the product of Example 1B (0.061 g, 50%). MS (ESI-) m/z 507 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.57 (s, 2H), 7.17 (dd, *J*=7.72, 4.78 Hz, 1H), 7.31 (m, 5H), 7.42 (t, *J*=7.54 Hz, 2H), 7.57 (m, 5H), 7.67 (d, *J*=8.09 Hz, 1H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.50 (dd, *J*=4.60, 2.02 Hz, 1H), 15.84 (s, 1H).

Example 60

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[2-(1H-indol-3-yl)ethyl]-1,8-

naphthyridin-2(1H)-one

Example 60A

ethyl 2-{[2-(1H-indol-3-yl)ethyl]amino}nicotinate

The title compound was prepared according to the procedure of Example 3A substituting tryptamine for 2-ethylbutylamine (1.24 g, 80%). MS (DCI) m/z 310 $(M+H)^+$.

Example 60B

1-[2-(1H-indol-3-yl)ethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 60A for the product of Example 3A (0.164 g, 53%). MS (DCI) m/z 325 $(M+NH_4)^+$.

Example 60C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[2-(1H-indol-3-yl)ethyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 60B for the product of Example 1B (0.140 g, 54%). MS (ESI-) m/z 484 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.09 (m, 2H), 4.75 (m, 2H), 7.08 (m, 2H), 7.27 (d, *J*=2.57 Hz, 1H), 7.36 (d, *J*=6.99 Hz, 1H), 7.54 (m, 2H), 7.77 (m, 3H), 7.94 (d, *J*=7.72 Hz, 1H), 8.60 (dd, *J*=8.09, 1.84 Hz, 1H), 8.95 (dd, *J*=4.78, 1.84 Hz, 1H), 10.88 (s, 1H).

Example 61

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-[(6-ethoxy-2-pyridinyl)methyl]-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 61A

1-[(6-chloro-2-pyridinyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-bromomethyl-6-chloropyridine for n-butyl bromide (0.159 g, 45%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.40 (s, 2H), 7.41 (m, 2H), 7.49 (d, *J*=7.72 Hz, 1H), 7.80 (t, *J*=7.72 Hz, 1H), 8.46 (dd, *J*=7.72, 1.84 Hz, 1H), 8.68 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 61B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-[(6-ethoxy-2-pyridinyl)methyl]-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 61A for the product of Example 1B (0.109 g, 42%). MS (ESI-) m/z 476 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.19 (t, *J*=6.99 Hz, 3H), 4.17 (q, *J*=6.99 Hz, 2H), 5.52 (s, 2H), 6.45 (d, *J*=7.35 Hz, 1H), 6.54 (d, *J*=7.72 Hz, 1H), 7.15 (m,

1H), 7.29 (t, *J*=7.72 Hz, 2H), 7.54 (m, 2H), 7.66 (d, *J*=8.09 Hz, 1H), 8.42 (m, 2H), 15.83 (s, 1H).

Example 62

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-7-methyl-1,8-naphthyridin-2(1H)-one

Example 62A

phenylmethanaminium 2-(benzylamino)-6-methylnicotinate

The title compound was prepared as a benzylamine salt according to the procedure of Example 3A substituting 2-chloro-6-methyl-nicotinic acid for 2-chloro-nicotinic acid ethyl ester and benzyl amine for 2-ethylbutylamine (0.480 g, 46 %). MS (ESI+) m/z 243.03 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.35 (s, 3H), 3.67 (s, 2H), 4.65 (s, 2H), 5.73 (br s, 3H), 6.16 (d, *J*=7.72 Hz, 1H), 7.17 (m, 10H), 7.76 (d, *J*=7.35 Hz, 1H), 8.66 (br s, 1H).

Example 62B

1-benzyl-7-methyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 62A for the product of Example 3A (0.150 g, 50 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.66 (s, 3H), 5.47 (s, 2H), 7.10 (d, *J*=8.09 Hz, 1H), 7.31 (m, 3H), 7.55 (dd, *J*=7.54, 1.65 Hz, 2H), 8.26 (d, *J*=8.09 Hz, 1H).

Example 62C

1-benzyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-7-methyl-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 62B for the product of Example 1B (0..53 g, 51 %). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.61 (s, 3H), 5.69 (s, 2H), 7.30 (m, 6H), 7.53 (m, 1H), 7.64 (m, *J*=7.35 Hz, 1H), 7.74 (t, *J*=7.54 Hz, 1H), 7.90 (d, *J*=8.82 Hz, 1H), 8.46 (d, *J*=8.46 Hz, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI+) m/z 447.0 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.48 (s, 3H), 5.50 (s, 2H), 7.25 (m, 7H), 7.54 (m, 1H), 7.66 (d, *J*=6.25 Hz, 1H), 8.28 (d, *J*=7.72 Hz, 1H), 15.95 (s, 1H).

Example 63

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(6-methyl-2-pyridinyl)methyl]-1,8-naphthyridin-2(1H)-one

Example 63A

1-[(6-methyl-2-pyridinyl)methyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-bromomethyl-6-methylpyridine for n-butyl bromide (0.088 g, 27%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.42 (s, 3H), 5.38 (s, 2H), 7.19 (d, *J*=7.72 Hz, 1H), 7.37 (m, 2H),

7.58 (t, J=7.72 Hz, 1H), 8.45 (dd, J=7.72, 1.84 Hz, 1H), 8.67 (dd, J=4.78, 1.84 Hz, 1H).

Example 63B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(6-methyl-2-pyridinyl)methyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 63A for the product of Example 1B (0.081 g, 40%). MS (ESI-) m/z 446 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.45 (s, 3H), 5.54 (s, 2H), 6.57 (d, J=7.72 Hz, 1H), 7.04 (d, J=7.35 Hz, 1H), 7.16 (dd, J=7.17, 4.96 Hz, 1H), 7.29 (t, J=7.72 Hz, 2H), 7.47 (t, J=7.72 Hz, 1H), 7.56 (m, 1H), 7.66 (d, J=7.72 Hz, 1H), 8.43 (m, 2H), 15.82 (s, 1H).

Example 64

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(1-ethylpropyl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 64A

ethyl 2-[(1-ethylpropyl)amino]nicotinate

The title compound was prepared according to the procedure of Example 3A substituting 2-ethyl-propyllamine for 2-ethylbutylamine (1.45 g, 88 %). MS (ESI+) 237.1 $(M+H)^+$. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, J=7.35 Hz, 6H), 1.38 (t, J=7.17 Hz, 3H), 1.60 (m, 4H), 4.17 (m, 1H), 4.32 (q, J=7.11 Hz, 2H), 6.45 (dd, J=7.72, 4.78 Hz, 1H), 7.89 (br d, J=8.09 Hz, 1H), 8.10 (dd, J=7.72, 1.84 Hz, 1H), 8.24 (dd, J=4.78, 2.21 Hz, 1H).

Example 64B

1-(1-ethylpropyl)-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 64A for the product of Example 3A (0.120 g, 57 %). MS (ESI+) m/z 223.1 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, J=7.54 Hz, 6H), 1.88 (m, 2H), 2.21 (s, 2H), 5.43 (s, 1H), 7.24 (dd, J=6.99, 4.04 Hz, 1H), 8.42 (dd, J=7.72, 1.84 Hz, 1H), 8.68 (dd, J=4.78, 1.84 Hz, 1H).

Example 64C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-(1-ethylpropyl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 64B for the product of Example 1B (0.030 g, 15 %). MS (ESI+) m/z 413.04 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.76 (t, J=7.54 Hz, 6H), 1.90 (m, 2H), 2.29 (m, 2H), 5.37 (m, 0.5H), 5.92 (m, 0.5H), 7.50 (m, 1H), 7.56 (t, J=7.54 Hz, 1H), 7.69 (m, 1H), 7.78 (t, J=7.17 Hz, 1H), 7.93 (d, J=7.35 Hz, 1H), 8.58 (d, J=8.09 Hz, 1H), 8.84 (m, 1H), 14.11 (s, 1H). The sodium salt of the title compound was prepared according

to the procedure of Example 1D. MS (ESI+) m/z 413.07 $(M+H-Na)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 0.74 (t, *J*=7.35 Hz, 6H), 1.88 (br s, 2H), 2.30 (br s, 2H), 5.35 (br s, 0.5H), 5.78 (br s, 0.5H), 7.28 (br s, 1H), 7.42 (m, *J*=7.35 Hz, 2H), 7.66 (m, 1H), 7.79 (br d, *J*=7.35 Hz, 1H), 8.47 (br d, *J*=7.35 Hz, 1H), 8.64 (br s, 1H).

Example 65

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(1S)-1-phenylethyl]-1,8-naphthyridin-2(1H)-one

Example 65A

ethyl 2-{[(1S)-1-phenylethyl]amino}nicotinate

The title compound was prepared according to the procedure of Example 3A substituting (S)-(-)-α-methylbenzylamine for 2-ethylbutylamine (2.2 g, 81%). MS (DCI) m/z 271 $(M+H)^+$.

Example 65B

1-[(1S)-1-phenylethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 65A for the product of Example 3A (0.320 g, 80%). ^1H NMR (300 MHz, DMSO-d_6) δ 1.86 (d, *J*=6.99 Hz, 3H), 6.65 (q, *J*=6.99 Hz, 1H), 7.27 (m, 3H), 7.40 (m, 3H), 8.43 (dd, *J*=7.72, 1.84 Hz, 1H), 8.73 (dd, *J*=4.96, 2.02 Hz, 1H).

Example 65C

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[(1S)-1-phenylethyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 65B for the product of Example 1B (0.122 g, 36%). MS (ESI-) m/z 445 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 1.90 (d, *J*=7.35 Hz, 3H), 6.87 (m, 1H), 7.12 (m, 2H), 7.25 (m, 6H), 7.55 (m, 1H), 7.65 (d, *J*=7.72 Hz, 1H), 8.40 (d, *J*=6.25 Hz, 2H), 15.92 (s, 1H).

Example 66

2-{2-[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]ethyl}-1H-isoindole-1,3(2H)-dione

Example 66A

1-[2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)ethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting N-(2-bromoethyl)phthalimide for n-butyl bromide (0.121 g, 20%). ^1H NMR (300 MHz, DMSO-d_6) δ 4.00 (t, *J*=5.52 Hz, 2H), 4.46 (t, *J*=5.52 Hz, 2H), 7.28 (dd, *J*=7.72, 4.78 Hz, 1H), 7.80 (s, 4H), 8.38 (dd, *J*=7.72, 1.84 Hz, 1H), 8.53 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 66B

2-{2-[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]ethyl}-1H-isoindole-1,3(2H)-dione

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 65B for the product of Example 1B (0.085 g, 46 %). MS (ESI-) m/z 514 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6/TFA) δ 4.09 (t, *J*=5.15 Hz, 2H), 4.87 (m, 2H), 7.11 (dd, *J*=7.91, 4.60 Hz, 1H), 7.19 (d, *J*=8.09 Hz, 1H), 7.44 (t, *J*=7.72 Hz, 1H), 7.58 (m, 5H), 7.84 (d, *J*=8.09 Hz, 1H), 8.34 (dd, *J*=4.41, 1.84 Hz, 1H), 8.42 (dd, *J*=7.91, 1.65 Hz, 1H).

Example 67

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(3-hydroxypropyl)-1,8-naphthyridin-2(1H)-one

A solution of the product of Example 73 in THF (5 mL) was reacted with sodium borohydride (0.022 g, 0.58 mmol) at 0 °C for 30 minutes. The solution was poured into water and extracted with ethyl acetate. The extract was dried over sodium sulfate, filtered, concentrated and purified by preparative HPLC on a Waters Symmetry C8 column (40mm x 100mm, 7μm particle size) using a gradient of 10% to 100% acetonitrile/0.1% aqueous TFA over 12minutes (15 minute run time) at a flow rate of 70mL/min to produce the title compound. MS (DCI/NH_3) m/z 401 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.87 (m, 2H), 3.54 (t, *J*=6.43 Hz, 2H), 4.55 (m, 2H), 7.52 (dd, *J*=8.09, 4.78 Hz, 1H), 7.56 (m, 1H), 7.71 (d, *J*=8.09 Hz, 1H), 7.79 (m, 1H), 7.94 (d, *J*=8.09 Hz, 1H), 8.58 (dd, *J*=8.09, 1.84 Hz, 1H), 8.90 (dd, *J*=4.60, 1.65 Hz, 1H), 14.13 (s, 1H).

Example 68

1-cyclopentyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 68A

ethyl 2-(cyclopentylamino)nicotinate

The title compound was prepared according to the procedure of Example 3A substituting cyclopentylamine for 2-ethylbutylamine (0.231 g, 67 %). MS (ESI+) m/z 235.1 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, *J*=7.17 Hz, 3H), 1.64 (m, 6H), 2.08 (m, 2H), 4.31 (q, *J*=7.23 Hz, 2H), 4.45 (m, 1H), 6.48 (dd, *J*=7.72, 4.78 Hz, 1H), 8.02 (d, *J*=5.88 Hz, 1H), 8.10 (dd, *J*=7.91, 2.02 Hz, 1H), 8.28 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 68B

1-cyclopentyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 68A for the product of Example 3A (0.130 g, 56 %). MS (ESI+) m/z 221.08 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.66 (m, 1H), 1.99 (m, 4H), 2.21

(m, 2H), 5.79 (m, 1H), 7.25 (dd, *J*=8.09, 4.78 Hz, 1H), 8.42 (dd, *J*=7.72, 2.21 Hz, 1H), 8.70 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 68C

1-cyclopentyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 68B for the product of Example 1B (0.133 g, 60 %). MS (ESI+) m/z 433.06 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.70 (m, 2H), 1.85 (m, 2H), 2.07 (s, 2H), 2.28 (m, 2H), 6.17 (m, *J*=8.64, 8.64 Hz, 1H), 7.52 (m, 2H), 7.65 (d, *J*=7.72 Hz, 1H), 7.77 (m, 1H), 7.93 (d, *J*=6.99 Hz, 1H), 8.57 (dd, *J*=7.91, 2.02 Hz, 1H), 8.86 (dd, *J*=4.78, 1.84 Hz, 1H), 14.05 (br s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.63 (m, 2H), 1.79 (br s, 2H), 2.04 (m, 2H), 2.23 (m, 2H), 6.08 (m, 1H), 7.31 (br s, 1H), 7.43 (br s, 2H), 7.65 (d, *J*=6.25 Hz, 1H), 7.80 (br s, 1H), 8.48 (d, *J*=7.72 Hz, 1H), 8.69 (br s, 1H).

Example 69

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-[2-(1,3-dioxolan-2-yl)ethyl]-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 69A

1-[2-(1,3-dioxolan-2-yl)ethyl]-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-(2-bromomethyl)-1,3-dioxolane for n-butyl bromide (0.86 g, 53%). MS (DCI/NH_3) m/z 265 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.98 (m, 2H), 3.83 (m, 4H), 4.25 (m, 2H), 4.92 (m, 1H), 7.38 (m, 1H), 8.39 (dd, *J*=7.72, 1.84 Hz, 1H), 8.78 (dd, *J*=4.96, 2.02 Hz, 1H).

Example 69B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1-[2-(1,3-dioxolan-2-yl)ethyl]-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 69A for the product of Example 1B (0.89 g, 62%). MS (DCI/NH_3) m/z 443 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.03 (m, 2H), 2.50 (m, 2H), 3.84 (m, 2H), 4.59 (m, 2H), 4.97 (t, *J*=4.60 Hz, 1H), 7.51 (dd, *J*=7.91, 4.60 Hz, 1H), 7.56 (m, 1H), 7.77 (m, 2H), 7.94 (m, 1H), 8.56 (dd, *J*=8.09, 1.84 Hz, 1H), 8.89 (dd, *J*=4.78, 1.84 Hz, 1H), 14.09 (s, 1H).

Example 70

1-(2,3-dihydroxypropyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The product of Example 55B (1.08g, 0.028 mol) was reacted with osmium tetroxide

(0.0007mol) and N-methylmorpholine N-oxide (4.96g, 0.043 mol) in a 1:1 mixture of water and THF (50 mL) at room temperature for 18 hours. The reaction mixture was treated with sodium bisulfite and diluted with water. The product precipitated from the aqueous mixture and was collected by vacuum filtration to give the title compound as a a white solid (1.09g, 93%). MS (DCI/NH_3) m/z 417 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 3.33 (m, 2H), 3.87 (m, 1H), 4.37 (m, 2H), 4.52 (t, *J*=6.07 Hz, 1H), 4.78 (d, *J*=5.52 Hz, 1H), 7.17 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 2H), 7.56 (m, 1H), 7.67 (d, *J*=6.99 Hz, 1H), 8.40 (dd, *J*=7.72, 1.84 Hz, 1H), 8.53 (dd, *J*=4.78, 1.84 Hz, 1H), 15.80 (m, 1H).

Example 71

1-cycloheptyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 71A

ethyl 2-(cycloheptylamino)nicotinate

The title compound was prepared according to the procedure of Example 3A substituting cycloheptylamine for 2-ethylbutylamine (1.01 g, 83 %). MS (ESI+) m/z 263.1 $(M+H)^+$. ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (t, *J*=7.17 Hz, 3H), 1.62 (m, 10H), 2.02 (m, 2H), 4.29 (m, 1H), 4.31 (q, *J*=7.35 Hz, 2H), 6.45 (dd, *J*=7.72, 4.78 Hz, 1H), 8.05 (d, *J*=6.99 Hz, 1H), 8.10 (dd, *J*=7.91, 2.02 Hz, 1H), 8.26 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 71B

1-cycloheptyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 71A for the product of Example 3A (0.205 g, 55 %). MS (ESI+) m/z 249.1 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 1.63 (m, 6H), 1.84 (m, 4H), 2.43 (m, 2H), 5.39 (s, 1H), 7.24 (dd, *J*=7.72, 4.78 Hz, 1H), 8.40 (m, 1H), 8.71 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 71C

1-cycloheptyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 71B for the product of Example 1B (0.041 g, 15 %). MS (ESI+) m/z 439.07 $(M+H)^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 1.23 (m, 6H), 1.58 (m, 4H), 1.79 (m, 2H), 5.90 (m, 1H), 7.45 (m, 1H), 7.53 (m, 1H), 7.66 (m, *J*=9.56 Hz, 1H), 7.74 (d, *J*=7.72 Hz, 1H), 7.90 (d, *J*=6.25 Hz, 1H), 8.54 (d, *J*=7.35 Hz, 1H), 8.85 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 1.61 (m, 8H), 1.77 (m, 4H), 1.94 (m, 2H), 5.60 (m, 1H), 7.10 (dd, *J*=7.54, 4.60 Hz, 1H), 7.54 (m, 1H), 7.66 (dd, *J*=7.72, 1.47 Hz, 1H), 8.36 (dd, *J*=7.72, 2.21 Hz, 1H), 8.51 (dd, *J*=4.78, 2.21 Hz, 1H), 15.99 (s, 1H).

Example 72

1-(3-anilinopropyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

A solution of the product of Example 73 (0.090 g, 0.23 mmol) and aniline (0.15 mL, 0.23 mmol) in THF (6 mL) was treated with sodium triacetoxyborohydride (0.08 g, 0.38 mmol) and glacial acetic acid (0.025 mL, 0.43 mmol) at ambient temperature for 24 hours. The solvent was removed under vacuum and the resulting solid was purified by preparative HPLC on a Waters Symmetry C8 column (40mm x 100mm, 7μm particle size) using a gradient of 10% to 100% acetonitrile/0.1% aqueous TFA over 12 minutes (15 minutes run time) at a flow rate of 70mL/min to give the title compound. MS (DCI/NH_3) m/z 476 $(M+H)^+$. The title compound was dissolved in 1,4-dioxane (6 mL) and 4M HCl in dioxane (2 mL). After stirring at room temperature for 3 hours, the mixture was filtered and the filter cake was dried to yield the hydrochloride salt. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.11 (m, 2H), 3.32 (m, 2H), 4.59 (t, J=6.80 Hz, 2H), 7.18 (s, 3H), 7.34 (d, J=7.35 Hz, 2H), 7.52 (m, 1H), 7.57 (m, 1H), 7.67 (d, J=7.35 Hz, 1H), 7.80 (m, 1H), 7.94 (d, J=7.72 Hz, 1H), 8.59 (dd, J=7.72, 1.84 Hz, 1H), 8.89 (dd, J=4.78, 1.84 Hz, 1H), 13.96 (s, 1H).

Example 73

3-[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]propanal

A stirred suspension of the product of Example 69B (0.65 g, 0.15 mmol) in water (3 mL) and glacial acetic acid (12 mL) at ambient temperature was treated dropwise with sulfuric acid (1 mL). The mixture was heated to 60 °C for 1 hour, and then diluted with water. The mixture was filtered and the filter cake was washed with water and dried to produce the title compound (0.455 g, 78%). MS (DCI/NH_3) m/z 399 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.72 (m, 2H), 4.59 (t, J=6.62 Hz, 2H), 7.17 (dd, J=7.72, 4.78 Hz, 1H), 7.28 (m, 1H), 7.55 (m, 1H), 7.67 (d, J=7.72 Hz, 1H), 8.39 (dd, J=7.72, 1.84 Hz, 1H), 8.52 (dd, J=4.78, 1.84 Hz, 1H), 9.76 (t, J=2.21 Hz, 1H), 9.76 (t, J=2.21 Hz, 1H).

Example 74

methyl 4-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}benzoate

Example 74A

methyl 4-[(2,4-dioxo-2H-pyrido[2,3-d][1,3]oxazin-1(4H)-yl)methyl]benzoate

The title compound was prepared according to the procedure of Example 1B substituting methyl 4-(bromomethyl)benzoate for n-butyl bromide (1.5 g, 75%). MS (DCI) m/z 313 $(M+H)^+$.

Example 74B

methyl 4-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-

naphthyridin-1(2H)-yl]methyl}benzoate

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 74A for the product of Example 1B (0.130 g, 37%). MS (ESI-) m/z 489 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.82 (s, 3H), 5.76 (s, 2H), 7.42 (d, J=8.09 Hz, 2H), 7.50 (m, 2H), 7.63 (d, J=7.72 Hz, 1H), 7.74 (t, J=7.72 Hz, 1H), 7.88 (d, J=8.46 Hz, 2H), 7.93 (m, 1H), 8.60 (dd, J=8.09, 1.84 Hz, 1H), 8.78 (d, J=3.31 Hz, 1H), 14.12 (br s, 1H).

Example 75

ethyl 5-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}-2-furoate

Example 75A

ethyl 5-[(2,4-dioxo-2H-pyrido[2,3-d][1,3]oxazin-1(4H)-yl)methyl]-2-furoate

The title compound was prepared according to the procedure of Example 1B substituting ethyl 5-chloromethyl-2-furancarboxylate for n-butyl bromide (0.073 g, 19%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.34 (t, J=7.17 Hz, 3H), 4.32 (q, J=7.35 Hz, 2H), 5.56 (s, 2H), 6.49 (d, J=3.68 Hz, 1H), 7.09 (d, J=3.31 Hz, 1H), 7.31 (dd, J=7.72, 4.78 Hz, 1H), 8.44 (dd, J=7.72, 1.84 Hz, 1H), 8.76 (dd, J=4.78, 1.84 Hz, 1H).

Example 75B

ethyl 5-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}-2-furoate

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 75A for the product of Example 1B (0.074 g, 69%). MS (DCI/NH_3) m/z 495 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.26 (t, J=7.17 Hz, 3H), 4.26 (q, J=7.23 Hz, 2H), 5.73 (s, 2H), 6.45 (d, J=3.68 Hz, 1H), 7.19 (d, J=3.68 Hz, 1H), 7.55 (m, 2H), 7.75 (m, 2H), 7.93 (d, J=7.72 Hz, 1H), 8.60 (dd, J=7.91, 1.83 Hz, 1H), 8.86 (dd, J=4.78, 1.84 Hz, 1H), 13.80 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.27 (t, J=7.17 Hz, 3H), 4.25 (q, J=7.23 Hz, 2H), 5.55 (s, 2H), 6.22 (d, J=3.31 Hz, 1H), 7.14 (d, J=3.31 Hz, 1H), 7.20 (dd, J=7.72, 4.60 Hz, 1H), 7.29 (m, 2H), 7.56 (m, 1H), 7.67 (d, J=8.09 Hz, 1H), 8.42 (dd, J=7.72, 2.20 Hz, 1H), 8.52 (dd, J=4.60, 2.21 Hz, 1H), 15.73 (s, 1H).

Example 76

1-[3-(dimethylamino)propyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

A solution of the product of Example 73 (0.085 g, 0.21 mmol) and dimethylamine (2.0 M in THF, 0.110 mL, 0.22 mmol) in tetrahyrofuran (4 mL) was reacted with sodium triacetoxyborohydride (0.06 g, 0.28 mmol) at room temperature for 1 hour. The solvent was removed under vacuum and the resulting solid was triturated with methanol and

dimethylsulfoxide (1:1), filtered, and dried to product the title compound (0.56 g, 61%). (DCI/NH_3) m/z 428 $(M+H)^+$.

The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.72 (m, 2H), 2.15 (s, 6H), 2.29 (t, *J*=7.17 Hz, 2H), 4.28 (m, 2H), 7.14 (dd, *J*=7.72, 4.78 Hz, 1H), 7.27 (m, 2H), 7.55 (ddd, *J*=8.27, 7.17, 1.47 Hz, 1H), 7.67 (dd, *J*=8.09, 1.47 Hz, 1H), 8.37 (dd, *J*=7.54, 2.02 Hz, 1H), 8.53 (dd, *J*=4.78, 1.84 Hz, 1H), 15.93 (s, 1H).

Example 77

1-{3-[[2-(dimethylamino)ethyl](methyl)amino]propyl}-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 72 substituting N,N,N-trimethylethylenediamine for aniline. MS (DCI/NH_3) m/z 485 $(M+H)^+$. The dihydrochloride salt of the title compound was prepared according to the procedure of Example 72. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.20 (s, 2H), 2.84 (m, *J*=4.41 Hz, 6H), 3.50 (m, 9H), 4.54 (m, 2H), 7.54 (m, 3H), 7.77 (m, 1H), 7.91 (d, *J*=8.09 Hz, 1H), 8.59 (dd, *J*=8.09, 1.84 Hz, 1H), 8.85 (dd, *J*=4.60, 1.65 Hz, 1H), 10.43 (s, 1H), 14.25 (s, 1H).

Example 78

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[3-(4-methyl-1-piperazinyl)propyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 72 substituting 4-methylpiperazine for aniline. MS (ESI-) m/z 450 $(M-H)^-$. The dihydrochloride salt of the title compound was prepared according to the procedure of Example 72. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.03 (m, 2H), 3.10 (m, 4H), 3.69 (m, 4H), 3.90 (m, 2H), 4.39 (s, 2H), 7.20 (dd, *J*=7.72, 4.41 Hz, 1H), 7.30 (m, 2H), 7.58 (m, 1H), 7.68 (d, *J*=7.72 Hz, 1H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.55 (dd, *J*=4.41, 1.84 Hz, 1H), 15.71 (s, 1H).

Example 79

1-(2-aminoethyl)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

A solution of Example 66 (45.0 mg, 0.087 mmol) in a mixture of absolute ethanol (1.5 mL), N,N-dimethylformamide (0.8 mL) and dimethyl sulfoxide (1.0 mL) was treated with hydrazine monohydrate (13.42 mg, 0.261 mmol) at room temperature. The mixture was then heated to reflux at 80 °C for 5 hours, cooled to room temperature, and concentrated. The concentrate was purified by a C8 HPLC column eluting with 20% to 80% acetonitrile in water with 1% trifluoroacetic acid to give the TFA salt of the title compound (0.010 g, 23%). MS (APCI+) m/z 386 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.20 (dd, *J*=11.95, 6.80 Hz, 2H), 4.62 (t, *J*=5.52 Hz, 2H), 7.27 (m, 1H), 7.39 (m, 2H), 7.65 (t, *J*=7.35 Hz, 1H), 7.75 (d, *J*=7.72 Hz, 1H), 7.82 (br s, 3H), 8.42 (d, *J*=9.56 Hz, 1H), 8.61 (d, *J*=3.31 Hz, 1H), 15.18 (br

s, 1H).

Example 80

1-[3-(diethylamino)propyl]-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 72 substituting diethylamine for aniline. MS (DCI/NH_3) m/z 456 $(M+H)^+$. The hydrochloride salt of the title compound was prepared according to the procedure of Example 72. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.19 (t, *J*=7.17 Hz, 6H), 2.15 (m, 2H), 3.12 (m, 6H), 4.55 (t, *J*=6.62 Hz, 2H), 7.57 (m, 2H), 7.66 (m, 1H), 7.80 (m, 1H), 7.95 (d, *J*=8.09 Hz, 1H), 8.61 (dd, *J*=7.72, 1.84 Hz, 1H), 8.90 (dd, *J*=4.60, 1.65 Hz, 1H), 10.05 (s, 1H), 13.92 (s, 1H).

Example 81

1-cyclohexyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 81A

ethyl 2-(cyclohexylamino)nicotinate

The title compound was prepared according to the procedure of Example 3A substituting cyclohexylamine for 2-ethylbutylamine (1.92 g, 61 %). MS (ESI+) m/z 249.1 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (m, 7H), 1.61 (m, 2H), 1.75 (m, 2H), 2.02 (m, 2H), 4.08 (m, 1H), 4.31 (q, *J*=7.11 Hz, 2H), 6.46 (dd, *J*=7.72, 4.78 Hz, 1H), 7.99 (d, *J*=7.72 Hz, 1H), 8.10 (dd, *J*=7.72, 2.21 Hz, 1H), 8.25 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 81B

1-cyclohexyl-2H-pyrido[2,3-d][1,3]oxazine-2,4(1H)-dione

The title compound was prepared according to the procedure of Example 3B substituting the product of Example 81A for the product of Example 3A (0.171 g, 35 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (m, 4H), 1.73 (m, 2H), 1.91 (m, 2H), 2.47 (ddd, *J*=24.82, 12.32, 3.31 Hz, 2H), 5.28 (tt, *J*=12.27, 3.72 Hz, 1H), 7.24 (dd, *J*=6.99, 4.04 Hz, 1H), 8.41 (dd, *J*=7.72, 2.21 Hz, 1H), 8.70 (dd, *J*=4.78, 2.21 Hz, 1H).

Example 81C

1-cyclohexyl-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 81B for the product of Example 1B (0.073 g, 26 %). MS (ESI+) m/z 425.04 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.25 (m, 4H), 1.76 (m, 4H), 1.91 (s, 2H), 5.64 (s, 1H), 7.48 (dd, *J*=8.09, 4.78 Hz, 1H), 7.55 (t, *J*=7.54 Hz, 1H), 7.69 (m,

J=8.09 Hz, 1H), 7.77 (m, 1H), 7.92 (d, J=8.09 Hz, 1H), 8.56 (dd, J=8.09, 1.84 Hz, 1H), 8.86 (d, J=2.21 Hz, 1H), 14.12 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI+) m/z 425.04 $(M+H)^+$, 447.1 $(M+Na)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.31 (m, 4H), 1.52 (d, J=10.66 Hz, 2H), 1.63 (m, 2H), 1.83 (m, J=12.50 Hz, 2H), 5.41 (t, J=11.03 Hz, 1H), 7.11 (dd, J=7.72, 4.78 Hz, 1H), 7.27 (m, 2H), 7.55 (m, 1H), 7.66 (d, J=6.62 Hz, 1H), 8.37 (dd, J=7.72, 2.21 Hz, 1H), 8.50 (dd, J=4.60, 2.02 Hz, 1H), 15.94 (s, 1H).

Example 82

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-[3-(4-morpholinyl)propyl]-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 72 substituting morpholine for aniline (0.053 g 60%). MS (ESI-) m/z 450 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.03 (m, 2H), 3.10 (m, 4H), 3.69 (m, 4H), 3.90 (m, 2H), 4.39 (s, 2H), 7.20 (dd, J=7.72, 4.41 Hz, 1H), 7.30 (m, 2H), 7.58 (m, 1H), 7.68 (d, J=7.72 Hz, 1H), 8.42 (dd, J=7.72, 1.84 Hz, 1H), 8.55 (dd, J=4.41, 1.84 Hz, 1H), 15.71 (s, 1H).

Example 83

5-{[3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-2-oxo-1,8-naphthyridin-1(2H)-yl]methyl}-2-furoic acid

A solution of the product of Example 75B (23 mg, 0.046 mmol) in THF (1 mL) was treated with 1N NaOH (0.2 mL) at room temperature. After 3 hours, the mixture was treated with H_2O (5 mL), adjusted to pH 4 with 1N HCl, and extracted with ethyl acetate (2 x 25 mL). The extracts were washed with saturated NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated. The resulting solid was purified by preparative HPLC on a Waters Symmetry C8 column (25mm x 100mm, 7μm particle size) using a gradient of 10% to 100% acetonitrile/0.1% aqueous TFA over 8 minutes (10 minute run time) at a flow rate of 40mL/min to give the title compound (0.039 g, 83%). MS (ESI-) m/z 465 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.72 (s, 2H), 6.42 (d, J=3.68 Hz, 1H), 7.11 (d, J=3.31 Hz, 1H), 7.53 (m, 2H), 7.68 (d, J=7.72 Hz, 1H), 7.76 (m, 1H), 7.92 (d, J=7.72 Hz, 1H), 8.60 (dd, J=8.09, 1.84 Hz, 1H), 8.86 (dd, J=4.78, 1.84 Hz, 1H), 13.90 (s, 1H).

Example 84

1-benzyl-3-(7-bromo-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 84A

2-amino-5-bromobenzenesulfonamide

The title compound was prepared from 4-bromoaniline using the procedure described

in *JCS Perkin 1*, 1979, 1043.

Example 84B

ethyl 1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxylate

To a slurry of sodium hydride (60%, 0.118 g, 2.95 mmol) in anhydrous dimethylacetamide (6 mL) at 0 °C under N_2 was added diethyl malonate (0.472 g, 2.95 mmol) dropwise over 5 minutes. The mixture was stirred at ambient temperature for 1 hour, reacted with the product of Example 15A (0.50 g, 1.97 mmol), and heated at 120 °C for 3 hours. The mixture was cooled to ambient temperature and partitioned between ethyl acetate and cold water, and adjusted to pH to 5 with 1 M HCl. The aqueous layer was extracted with ethyl acetate (2 x 100 mL) and the combined extracts were washed with brine, dried over magnesium sulfate, filtered, and concentrated under vacuum. The residue was recrystallized from methanol to give the title compound as a white solid (0.439 g, 68 %). MS (ESI+) m/z 325.0 $(M+H)^+$, 347.0 $(M+Na)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.30 (t, *J*=7.17 Hz, 3H), 4.32 (q, *J*=7.23 Hz, 2H), 5.55 (s, 2H), 7.23 (m, 5H), 7.37 (dd, *J*=7.91, 4.60 Hz, 1H), 8.45 (dd, *J*=7.91, 2.02 Hz, 1H), 8.71 (dd, *J*=4.78, 1.84 Hz, 1H), 13.00 (s, 1H).

Example 84C

N-[2-(aminosulfonyl)-4-bromophenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The product of Example 84B (0.065 g, 0.20 mmol) was reacted with the product of Example 84A (0.050 g, 0.20 mmol) in toluene (4 mL) at reflux for 3 hours. The reaction was cooled and the resulting precipitate was collected by filtration and dried to give to give the title compound as an off-white solid (0.074 g, 70 %). MS (ESI+) m/z 528.9 $(M+H)^+$, 530.9 $(M+H)^+$, 551.1 $(M+Na)^+$, 552.9 $(M+Na)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.67 (s, 2H), 7.23 (m, 2H), 7.29 (m, 3H), 7.48 (dd, *J*=8.09, 4.78 Hz, 1H), 7.69 (s, 2H), 7.87 (dd, *J*=8.82, 2.21 Hz, 1H), 7.97 (m, 1H), 8.01 (d, *J*=2.21 Hz, 1H), 8.55 (dd, *J*=7.91, 1.65 Hz, 1H), 8.82 (dd, *J*=4.60, 1.65 Hz, 1H), 12.44 (s, 1H), 16.45 (s, 1H).

Example 84D

1-benzyl-3-(7-bromo-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

A mixture of the product of Example 84C (0.074 g, 0.14 mmol) in aqueous potassium hydroxide (10%, 5 mL) was heated to reflux for 16 hours, cooled to room temperature and adjusted to pH 3 with 6 M HCl. The mixture was filtered and the filter cake was washed with water, triturated with tetrahydrofuran/water, filtered, and dried under vacuum to give the title compound (0.060 g, 84 %). MS (ESI+) m/z 511.0 $(M+H)^+$, 512.9 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.62 (s, 2H), 7.21 (m, 1H), 7.27 (m, *J*=4.41 Hz, 5H), 7.36 (m, 1H), 7.50 (d, *J*=8.82 Hz, 1H), 7.84 (dd, *J*=8.82, 1.84 Hz, 1H), 7.95 (s, 1H), 8.51 (dd, *J*=7.91, 1.65 Hz, 1H), 8.68 (m, 1H). The sodium salt of the title compound was prepared according to the

procedure of Example 1D. MS (ESI+) m/z 511.0 $(M+H-Na)^+$, 512.9 $(M+H-Na)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 5.52 (s, 2H), 7.17 (m, 2H), 7.24 (m, 5H), 7.71 (m, 1H), 7.76 (d, *J*=2.21 Hz, 1H), 8.40 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.60, 2.02 Hz, 1H), 16.09 (s, 1H).

Example 85

1-benzyl-3-(1,1-dioxido-7-phenyl-2H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 85A

N-[3-(aminosulfonyl)-1,1'-biphenyl-4-yl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-5-phenylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.084 g, 79 %). MS (ESI+) m/z 527.1 $(M+H)^+$, 549.1 $(M+Na)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 5.68 (s, 2H), 7.2-7.8 (m, 13H), 7.98 (s, 1H), 8.09 (s, 1H), 8.17 (s, 1H), 8.54 (s, 1H), 8.81 (s, 1H), 12.49 (s, 1H), 16.67 (s, 1H).

Example 85B

1-benzyl-3-(1,1-dioxido-7-phenyl-2H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 85A for the product of Example 84C (0.055 g, 69 %). MS (ESI+) m/z 509.1 $(M+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 5.71 (s, 2H), 7.24 (m, 1H), 7.30 (m, 3H), 7.49 (m, 4H), 7.79 (m, *J*=7.35 Hz, 3H), 8.07 (m, *J*=11.03, 2.21 Hz, 2H), 8.60 (dd, *J*=7.91, 1.65 Hz, 1H), 8.81 (m, *J*=3.68 Hz, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI+) m/z 531.0 (M+), 509.1 $(M-Na+H)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 5.53 (s, 2H), 7.17 (m, 2H), 7.25 (m, *J*=4.41 Hz, 4H), 7.39 (m, 2H), 7.49 (t, *J*=7.54 Hz, 2H), 7.71 (d, *J*=6.99 Hz, 2H), 7.89 (m, 2H), 8.42 (dd, *J*=7.72, 1.84 Hz, 1H), 8.49 (dd, *J*=4.60, 2.02 Hz, 1H), 15.99 (s, 1H).

Example 86

1-benzyl-3-(7-cyclohexyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 86A

2-amino-5-cyclohexylbenzenesulfonamide

A solution of 4-cyclohexylaniline (0.877 g, 5.0 mmol, 1.0 eq) in nitroethane (5 mL) was cooled to –40 °C, treated dropwise with chlorosulfonyl isocyanate (0.87 g, (0.523 mL, 6.15 mmol, 1.23 eq), warmed to 0 °C, treated with aluminum trichloride (0.85 g, 6.35 mmol, 1.27 eq), heated in a 110 °C oil bath for 30 minutes, cooled to ambient temperature, and

poured into 200 mL of ice water. The mixture was filtered and the filter cake was rinsed with cold water, dissolved in 50% H_2SO_4 (25 mL), heated to reflux for 4 hours, cooled to ambient temperature, poured into 200 mL of ice water, and carefully neutralized to pH 7 with 40% NaOH. The reaction mixture was extracted with ethyl acetate (3 x 100 mL) and the combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated to give 0.40 g of the desired product (31% yield). MS (ESI+) m/z 255.0 $(M+H)^+$, 272.1 $(M+H_2O)^+$, 277.0 $(M+Na)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.32 (m 4H), 1.71 (m, 6H), 2.36 (m, 1H), 5.64 (s, 2H), 6.72 (d, *J*=8.09 Hz, 1H), 7.11 (dd, *J*=8.46, 2.21 Hz, 1H), 7.16 (s, 2H), 7.38 (d, *J*=2.21 Hz, 1H).

Example 86B

N-[2-(aminosulfonyl)-4-cyclohexylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting the product of Example 86A for 2-amino-5-bromobenzenesulfonamide (0.081 g, 76 %). MS (ESI+) m/z 533.1 $(M+H)^+$, 555.2 $(M+Na)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.27 (m, 1H), 1.45 (m, 4H), 1.72 (m, 1H), 1.85 (m, 4H), 2.61 (m, 1H), 5.68 (s, 2H), 7.26 (m, 4H), 7.50 (m, 4H), 7.76 (d, *J*=1.84 Hz, 1H), 7.86 (d, *J*=8.46 Hz, 2H), 8.54 (dd, *J*=8.09, 1.47 Hz, 1H), 8.80 (s, 1H), 12.31 (s, 1H), 16.78 (s, 1H).

Example 86C

1-benzyl-3-(7-cyclohexyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 86B for the product of Example 84C (0.040 g, 53 %). MS (ESI+) m/z 533.1 $(M+H+H_2O)^+$, 555.1 $(M+H_2O+Na)^+$, 515.1 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.34 (m, 5H), 1.77 (m, 5H), 2.60 (m, 1H), 5.66 (s, 2H), 7.25 (m, 4H), 7.51 (m, *J*=9.56 Hz, 4H), 7.88 (s, 1H), 8.54 (s, 1H), 8.80 (s, 1H), 12.31 (s, 1H), 16.78 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.41 (m, 5H), 1.70 (m, 5H), 3.79 (m, 1H), 5.52 (s, 2H), 7.12 (dd, *J*=7.54, 4.60 Hz, 1H), 7.17 (m, 1H), 7.23 (m, 4H), 7.41 (dd, *J*=8.64, 2.02 Hz, 1H), 7.67 (d, *J*=2.21 Hz, 1H), 8.33 (d, *J*=8.46 Hz, 1H), 8.38 (dd, *J*=7.72, 1.84 Hz, 1H), 8.43 (dd, *J*=4.60, 2.02 Hz, 1H), 11.15 (s, 1H).

Example 87

1-benzyl-3-(7-tert-butyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 87A

N-[2-(aminosulfonyl)-4-tert-butylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-5-tert-butylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.072 g, 79 %). MS (ESI+) m/z 507.12 $(M+H)^+$, 524.2 $(M+H_2O)^+$, 529.1 $(M+Na)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 1.33 (s, 9H), 5.68 (s, 2H), 7.22 (m, 1H), 7.29 (m, *J*=3.68 Hz, 4H), 7.47 (m, 3H), 7.70 (dd, *J*=8.64, 2.39 Hz, 1H), 7.88 (d, *J*=8.82 Hz, 1H), 7.91 (d, *J*=2.21 Hz, 1H), 8.54 (dd, *J*=8.09, 1.84 Hz, 1H), 8.81 (dd, *J*=4.60, 1.65 Hz, 1H), 12.33 (s, 1H), 16.79 (s, 1H).

Example 87B

1-benzyl-3-(7-tert-butyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 87A for the product of Example 84C (0.040 g, 100 %). MS (ESI+) m/z 489.1 $(M+H)^+$, 511.1 $(M+Na)^+$; ^1H NMR (300 MHz, DMSO-d_6) δ 1.34 (s, 9H), 5.70 (s, 2H), 7.22 (m, 1H), 7.29 (m, *J*=4.41 Hz, 4H), 7.48 (m, 1H), 7.59 (d, *J*=8.82 Hz, 1H), 7.75 (s, 1H), 7.81 (d, *J*=10.66 Hz, 1H), 8.58 (d, *J*=6.62 Hz, 1H), 8.79 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO-d_6) δ 1.32 (s, 9H), 5.53 (s, 2H), 7.18 (m, 2H), 7.25 (m, *J*=4.41 Hz, 5H), 7.59 (s, 1H), 7.65 (m, 1H), 8.42 (d, *J*=7.35 Hz, 1H), 8.50 (m, *J*=3.86, 2.02 Hz, 1H).

Example 88

1-benzyl-4-hydroxy-3-(7-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

Example 88A

N-[2-(aminosulfonyl)-4-methylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-5-methylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.075 g, 90 %). MS (ESI+) m/z 465.1 $(M+H)^+$, 482.0 $(M+H_2O)^+$, 487.1 $(M+Na)^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 2.39 (s, 3H), 5.68 (s, 2H), 7.23 (m, 1H), 7.29 (m, 4H), 7.47 (m, 4H), 7.73 (d, *J*=1.47 Hz, 1H), 7.84 (d, *J*=8.09 Hz, 1H), 8.54 (dd, *J*=7.72, 1.84 Hz, 1H), 8.81 (dd, *J*=4.60, 1.65 Hz, 1H), 12.30 (s, 1H), 16.78 (s, 1H).

Example 88B

1-benzyl-4-hydroxy-3-(7-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 88A for the product of Example 84C (0.031 g, 42 %). MS (ESI+) m/z 447.0 $(M+H)^+$, 469.1 $(M+Na)^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 2.41 (s,

3H), 5.65 (s, 2H), 7.24 (m, 5H), 7.45 (m, 3H), 7.66 (s, 1H), 8.54 (d, J=7.72 Hz, 1H), 8.72 (s, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.37 (s, 3H), 5.55 (s, 2H), 7.21 (m, 7H), 7.41 (d, J=8.46 Hz, 1H), 7.51 (s, 1H), 8.43 (d, J=8.09 Hz, 1H), 8.53 (s, 1H).

Example 89

1-butyl-3-(6-chloro-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 89A

ethyl 1-butyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxylate

To a slurry of NaH (95%, 0.44 g, 18.2 mmol) in 15 mL anhydrous DMA at 10 °C under N_2 was added diethyl malonate (2.9 g, 18.2 mmol) dropwise over 10 minutes. The mixture was stirred at ambient temperature for 30 minutes, treated with the product of Example 1B (2.0 g, 9.1 mmol) and heated at 120 °C for 3 hours. The mixture was cooled to ambient temperature and partitioned between ethyl acetate and cold water adjusting the pH to 5 with 1 M HCl. The organic layer was washed 2 x 100 mL with water, 2 x 100 mL with saturated brine, dried (Na_2SO_4), filtered and the filtrate was concentrated under vacuum. The residue was recrystallized from hexane/ethyl acetate to give the desired compound as a white solid (1.84 g, 70% yield). MS (APCI+) m/z 291 $(M+H)^+$.

Example 89B

N-[2-(aminosulfonyl)-4-chlorophenyl]-1-butyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

A mixture of the product of Example 89A (87 mg, 0.3 mmol) and 2-amino-4-chlorobenzenesulfonamide (62 mg, 0.3 mmol) in toluene (5 mL) was refluxed for 16 hours, cooled, and the resulting precipitate was collected by filtration and dried to give the desired amide as an off-white solid (80 mg, 59% yield).
MS (APCI+) m/z 451 $(M+H)^+$.

Example 89C

ethyl 1-butyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxylate

The title compound was prepared according to the procedure of Example 84C substituting the product of Example 89B for the product of Example 84B (0.037 g, 53%). MS (ESI-) m/z 431 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.93 (t, J=7.17 Hz, 3H), 1.34 (m, 2H), 1.58 (m, 2H), 4.27 (m, 2H), 7.14 (dd, J=7.72, 4.78 Hz, 1H), 7.32 (dd, J=8.27,

2.02 Hz, 1H), 7.42 (d, J=1.84 Hz, 1H), 7.68 (d, J=8.46 Hz, 1H), 8.37 (dd, J=7.54, 2.02 Hz, 1H), 8.54 (dd, J=4.78, 1.84 Hz, 1H), 16.09 (s, 1H).

Example 90

1-benzyl-3-(8-bromo-5-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 90A

N-[2-(aminosulfonyl)-3-bromo-6-methylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-6-bromo-3-methylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide to give the crude title compound (0.1 g, 98%).

Example 90B

1-benzyl-3-(8-bromo-5-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 90A for the product of Example 84C. The crude product was purified by column chromatography with silica gel eluting with dichloromethane and methanol (98:2) to give the title compound as a white solid, (0.03 g, 31% yield). MS (ESI-) m/z 525 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 16.0 (br s, 1H), 8.49 (dd, J=4.8, 1.8 Hz, 1H), 8.44 (dd, J=7.7, 1.8 Hz, 1H), 7.45 (br s, 1H), 7.37 (m, 1H), 7.23 (m, 3H), 7.16 (dd, J=4.8, 3.3 Hz, 1H), 7.01 (m, 1H), 6.85 (d, J=7.7 Hz, 1H), 5.53 (br s, 2H), 2.43 (s, 3H).

Example 91

1-benzyl-3-(8-fluoro-5-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 91A

N-[2-(aminosulfonyl)-3-fluoro-6-methylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-6-fluoro-3-methylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide to give the crude title compound (0.120 g, 100%).

Example 91B

1-benzyl-3-(8-fluoro-5-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 91A for the product of Example 84C. The crude product was purified by column chromatography with silica gel eluting with dichloromethane and methanol (98:2) as a white solid, (0.05 g, 44% yield). MS (ESI-) m/z 463 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 16.1 (br s, 1H), 8.49 (dd, *J*=4.6, 2.0 Hz, 1H), 8.44 (dd, *J*=7.7, 1.8 Hz, 1H), 7.59 (m, 1H), 7.47 (dd, *J*=7.3, 5.8 Hz, 1H), 7.38 (m, 1H), 7.21 (m, 3H), 7.16 (dd, *J*=7.7, 5.8 Hz, 1H), 6.99 (t, *J*=8.8 Hz, 1H), 5.53 (s, 2H), 2.42 (s, 3H).

Example 92

1-benzyl-4-hydroxy-3-(5-isopropyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

Example 92A

N-[2-(aminosulfonyl)-6-isopropylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-3-isopropylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.050 g, 55 %) after chromatrography on silica gel (eluting with 4:1 hexane/ethyl acetate). ^{1}H NMR (300 MHz, DMSO-d_6) δ ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.12 (d, *J*=6.62 Hz, 3H), 1.26 (d, *J*=6.99 Hz, 3H), 3.06 (m, 1H), 5.69 (m, 2H), 7.27 (m, 5H), 7.39 (s, 2H), 7.48 (dd, *J*=7.72, 4.78 Hz, 1H), 7.55 (t, *J*=7.72 Hz, 1H), 7.71 (d, *J*=8.09 Hz, 1H), 7.80 (dd, *J*=7.72, 1.10 Hz, 1H), 8.53 (dd, *J*=7.91, 1.65 Hz, 1H), 8.83 (dd, *J*=4.78, 1.84 Hz, 1H), 11.75 (s, 1H), 16.83 (s, 1H).

Example 92B

1-benzyl-4-hydroxy-3-(5-isopropyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 92a for the product of Example 84C (0.038 g, 75 %). MS (ESI+) m/z 475.1 $(M+H)^+$, 492.1 $(M+H_2O)^+$, 497.1 $(M+Na)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.34 (d, *J*=6.62 Hz, 6H), 3.30 (m, 1H), 5.73 (s, 2H), 7.27 (m, 5H), 7.54 (m, 2H), 7.78 (m, *J*=16.18, 7.72 Hz, 2H), 8.62 (dd, *J*=7.91, 1.65 Hz, 1H), 8.84 (s, 1H), 14.64 (s,

1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.32 (d, *J*=6.62 Hz, 6H), 3.42 (m, 1H), 5.53 (s, 2H), 7.15 (m, 2H), 7.25 (m, *J*=4.41 Hz, 4H), 7.29 (m, 1H), 7.53 (m, *J*=7.72, 1.84 Hz, 2H), 8.46 (m, 2H), 16.06 (s, 1H).

Example 93

1-benzyl-4-hydroxy-3-(5-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

Example 93A

N-[2-(aminosulfonyl)-6-methylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-3-methylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.059 g, 100 %). ^{1}H NMR (300 MHz, DMSO-d6) δ 2.27 (s, 3 H) 5.68 (m, 2 H) 7.24 (m, 5 H) 7.46 (m, 4 H) 7.59 (d, *J*=6.99 Hz, 1 H) 7.79 (d, *J*=7.72 Hz, 1 H) 8.54 (dd, *J*=8.09, 1.84 Hz, 1 H) 8.83 (dd, *J*=4.78, 1.84 Hz, 1 H) 11.90 (s, 1 H) 16.79 (s, 1 H).

Example 93B

1-benzyl-4-hydroxy-3-(5-methyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 93A for the product of Example 84C (0.015 g, 25 %) after silica gel chromatography (eluting with 98:2 dichloromethane/methanol). MS (ESI+) m/z 447.0 $(M+H)^+$, 469.1 $(M+Na)^+$. ^{1}H NMR (300 MHz, -d6) δ 2.52 (m, 3 H) 5.75 (m, 2 H) 7.23 (m, 1 H) 7.30 (m, 4 H) 7.47 (t, *J*=7.72 Hz, 1 H) 7.53 (dd, *J*=8.09, 4.78 Hz, 1 H) 7.69 (d, *J*=7.35 Hz, 1 H) 7.79 (d, *J*=8.09 Hz, 1 H) 8.63 (dd, *J*=7.72, 1.84 Hz, 1 H) 8.85 (dd, *J*=4.78, 1.84 Hz, 1 H) 14.41 (s, 1 H). The sodium salt of the title compound was prepared according to the procedure of Example 1d. ^{1}H NMR (300 MHz, DMSO-d6) δ 2.48 (s, 3 H) 5.56 (s, 2 H) 7.21 (m, 6 H) 7.49 (d, *J*=7.35 Hz, 1 H) 7.56 (d, *J*=7.35 Hz, 1 H) 8.47 (d, *J*=7.72 Hz, 1 H) 8.53 (s, 1 H) 11.98 (s, 1 H).

Example 94

1-benzyl-3-(5-bromo-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 94A

N-[2-(aminosulfonyl)-6-bromophenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-3-methylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.080 g, 25 %) after silica gel chromatography (eluting with 2:1 hexane/ethyl acetate). MS (ESI+) m/z 529.0 $(M+H)^+$, 530.9 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d6) δ 5.71 (m, 2 H) 7.23 (m, 1 H) 7.32 (m, 4 H) 7.50 (m, 2 H) 7.62 (s, 2 H) 7.96 (dd, *J*=7.91, 1.29 Hz, 1 H) 8.02 (dd, *J*=7.91, 1.29 Hz, 1 H) 8.55 (dd, *J*=7.91, 1.65 Hz, 1 H) 8.85 (dd, *J*=4.78, 1.84 Hz, 1 H) 11.95 (s, 1 H) 16.51 (s, 1 H).

Example 94B

1-benzyl-3-(5-bromo-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 94A for the product of Example 84C (0.040 g, 54 %). MS (ESI+) m/z 510.9 $(M+H)^+$, 512.9 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d6) δ 5.56 (s, 2 H) 7.23 (m, 8 H) 7.76 (d, *J*=8.46 Hz, 1 H) 7.94 (d, *J*=8.09 Hz, 1 H) 8.46 (dd, *J*=7.72, 1.84 Hz, 1 H) 8.55 (m, 1 H) 16.17 (s, 1 H). The sodium salt of the title compound was prepared according to the procedure of Example 1d. ^{1}H NMR (300 MHz, DMSO-d6) δ 5.53 (s, 2 H) 7.17 (m, 2 H) 7.25 (m, 5 H) 7.71 (d, *J*=6.99 Hz, 1 H) 7.90 (m, 1 H) 8.43 (dd, *J*=7.72, 1.84 Hz, 1 H) 8.49 (dd, *J*=4.60, 2.02 Hz, 1 H) 16.38 (s, 1 H).

Example 95

1-benzyl-3-(1,1-dioxido-5-propyl-2H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 95A

N-[2-(aminosulfonyl)-6-propylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-3-propylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.062 g, 59%). MS (DCI/NH_3) m/z 493 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.83 and 0.93 (two t, *J*=7.35 Hz, 3H), 1.57 (m, 2H), 2.57 (m, 2H), 5.66 (m, 2H), 7.28 (m, 5H), 7.41 (s, 2H), 7.48 (m, 2H), 7.61 (m, 1H), 7.81 (dd, *J*=7.72, 1.47 Hz, 1H), 8.53 (dd, *J*=7.91, 1.65 Hz, 1H), 8.83 (dd, *J*=4.78, 1.84 Hz, 1H), 11.82 (s, 1H), 16.80 (s, 1H).

Example 95B

1-benzyl-3-(1,1-dioxido-5-propyl-2H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 95A for the product of Example 84C (0.029 g, 50%). MS (ESI-) m/z 473 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.03 (t, *J*=7.17 Hz, 3H), 1.68 (m, 2H), 2.83 (t, *J*=7.72 Hz, 2H), 5.53 (s, 2H), 7.19 (m, 7H), 7.44 (d, *J*=6.25 Hz, 1H), 7.53 (d, *J*=7.35 Hz, 1H), 8.43 (dd, *J*=7.54, 1.84 Hz, 1H), 8.48 (dd, *J*=4.78, 1.84 Hz, 1H), 16.02 (s, 1H).

Example 96

1-benzyl-3-(5-ethyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 96A

N-[2-(aminosulfonyl)-6-ethylphenyl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 2-amino-3-ethylbenzenesulfonamide for 2-amino-5-bromobenzenesulfonamide (0.070 g, 74%). MS (ESI-) m/z 479 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.17 (t, *J*=7.54 Hz, 3H), 2.61 (q, *J*=7.60 Hz, 2H), 5.70 (m, 2H), 7.27 (m, 5H), 7.42 (s, 2H), 7.49 (m, 2H), 7.63 (m, 1H), 7.81 (dd, *J*=7.91, 1.29 Hz, 1H), 8.53 (dd, *J*=7.91, 1.65 Hz, 1H), 8.83 (dd, *J*=4.41, 1.84 Hz, 1H), 11.82 (s, 1H), 16.80 (s, 1H).

Example 96B

1-benzyl-3-(5-ethyl-1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 96A for the product of Example 84C (0.060 g, 93%). MS (ESI-) m/z 459 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.30 (t, *J*=7.54 Hz, 3H), 2.86 (q, *J*=7.35 Hz, 2H), 5.53 (s, 2H), 7.14 (dd, *J*=7.72, 4.78 Hz, 1H), 7.22 (m, 6H), 7.46 (d, *J*=7.72 Hz, 1H), 7.53 (d, *J*=7.72 Hz, 1H), 8.44 (dd, *J*=7.72, 1.84 Hz, 1H), 8.48 (dd, *J*=4.78, 1.83 Hz, 1H), 15.98 (s, 1H).

Example 97

3-(1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridin-3-yl)-2H-1,2,4-benzothiadiazine-

5-carbonitrile 1,1-dioxide

The product of Example 94B (0.329 g, 0.643 mmol) and CuCN (0.29 g, 3.21 mmol) in anhydrous DMF (5 mL) were heated under N_2 at 145° for 22 hrs. The reaction was cooled to room temperature, diluted with CH_2Cl_2 (50 mL) and 1N aq HCl (10 mL), and vigorously stirred for 15 minutes. The layers were separated and the aqueous phase extracted with CH_2Cl_2 (2x50 mL). The organic extracts were washed with 1N aqueous HCl (20 mL) and saturated aqueous NaCl, then dried over anhydrous Na_2SO_4. After filtration and concentration by rotary evaporation, the residue was purified by silica gel flash chromatography (2.5x14 cm, 5% EtOAc/CH_2Cl_2) to give the title compound (0.136 g, 46%). MS (ESI-) m/z 456 $(M-H)^-$. ^1H NMR (300 MHz, DMSO-d6) δ 5.69 (s, 2 H) 7.26 (m, 5 H) 7.47 (dd, *J*=7.91, 4.60 Hz, 1 H) 7.62 (t, *J*=7.91 Hz, 1 H) 8.25 (m, 2 H) 8.59 (dd, *J*=7.91, 2.02 Hz, 1 H) 8.80 (dd, *J*=4.60, 1.65 Hz, 1 H) 15.67 (s, 1 H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^1H NMR (300 MHz, DMSO- d_6) δ 5.53 (s, 2 H) 7.20 (m, 6 H) 7.41 (t, *J*=7.91 Hz, 1 H) 8.00 (d, *J*=7.35 Hz, 1 H) 8.07 (d, *J*=7.72 Hz, 1 H) 8.43 (dd, *J*=7.54, 1.65 Hz, 1 H) 8.51 (dd, *J*=4.60, 1.65 Hz, 1 H) 17.35 (s, 1 H).

Example 98

1-butyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-2(1H)-quinolinone

Example 98A

3-nitropyridine-2-thiol

2-mercapto-3-nitropyridine was prepared by treating 3-nitro-2-chloro-pyridine (50g, 0.0317 mol) with thiourea (24g, 0.0317mol) in 200 mL of ethanol at reflux for several hours. After the reaction mixture was allowed to cool, 7.19 mL solution of KOH (42.8g in 115 mL of water) was added and the resulting mixture was heated at reflux for 3 hours. The crude reaction mixture was cooled to room temperature and then concentrated to 50% of its volume in vacuo. After diluting with 300 mL of water, the product was isolated by vacuum filtration as an orange solid that was used without further purification. MS (DCI/NH_3) m/z 157 $(M+H)^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 5.76 (m, 1H), 7.67 (dd, *J*=8.46, 4.78 Hz, 1H), 8.63 (dd, *J*=8.46, 1.47 Hz, 1H), 8.73 (dd, *J*=4.60, 1.65 Hz, 1H).

Example 98B

3-aminopyridine-2-sulfonamide

The title compound, (3-aminopyrid-2-yl)sulfonamide was prepared in 3 steps (80% yield) from 2-mercapto-3-nitropyridine according to the procedure of R. Lejeune and co-workers as described in *J.pharm. Belg.*, 39, 217-224, 1984. MS (DCI/NH_3) m/z 174 $(M+H)^+$.

^{1}H NMR (300 MHz, DMSO-d_6) δ 6.00 (s, 2H), 7.25 (m, 2H), 7.34 (s, 2H), 7.82 (dd, *J*=4.04, 1.47 Hz, 1H).

Example 98C

N-[2-(aminosulfonyl)pyridin-3-yl]-1-butyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxamide

The title compound was prepared according to the procedure of Example 89B substituting 3-amino-pyridine-2-sulfonamide for 2-amino-4-chlorobenzenesulfonamide.

Example 98D

1-butyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-2(1H)-quinolinone

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 98C for the product of Example 84C .as a white solid (0.065 g, 22%). MS (ESI-) m/z 397 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.96 (t, *J*=7.35 Hz, 3H), 1.46 (m, 2H), 1.66 (m, 2H), 4.34 (m, 2H), 7.46 (t, *J*=7.54 Hz, 1H), 7.82 (m, 3H), 8.23 (d, *J*=6.99 Hz, 1H), 8.26 (d, *J*=7.72 Hz, 1H), 8.70 (d, *J*=3.68 Hz, 1H), 14.38 (s, 1H), 15.12 (s, 1H).

Example 99

1-benzyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-2(1H)-quinolinone

Example 99A

ethyl 1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxylate

The title compound was prepared according to the procedure of Example 84B substituting 1-benzyl-1H-benzo[d][1,3]oxazine-2,4-dione for the product of Example 15A.

Example 99B

N-[2-(aminosulfonyl)pyridin-3-yl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting the product of Example 99A for the product of Example 84B and substituting (3-amino-pyrid-2-yl)sulfonamide for 2-amino-5-bromobenzenesulfonamide to give the crude product as an off white solid.

Example 99C

1-benzyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-2(1H)-

quinolinone

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 99B for the product of Example 84C (0.076 g, 38%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.64 (s, 2H), 7.29 (m, 5H), 7.43 (m, *J*=7.72, 7.72 Hz, 1H), 7.54 (d, *J*=8.46 Hz, 1H), 7.80 (m, 2H), 8.23 (m, 2H), 8.69 (d, *J*=3.31 Hz, 1H).

Example 100

1-benzyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

Example 100A

N-[2-(aminosulfonyl)pyridin-3-yl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting 3-amino-pyridine-2-sulfonamide for 2-amino-5-bromobenzenesulfonamide. MS (ESI-) m/z 452 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.66 (s, 2H), 7.22 (m, 1H), 7.28 (m, 3H), 7.43 (m, 1H), 7.70 (m, 3H), 8.52 (m, 2H), 8.77 (s, 3H), 12.56 (s, 1H), 16.34 (s, 1H).

Example 100B

1-benzyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 100A for the product of Example 84C to give after purification by reverse phase HPLC (water/acetonitrile/0.1%NH_4OAc gradient) the title compound as a white solid (0.053 g, 10%). MS (ESI-) m/z 432 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.70 (m, 2H), 7.25 (m, 7H), 7.50 (dd, *J*=7.91, 4.60 Hz, 1H), 7.80 (dd, *J*=8.46, 4.41 Hz, 1H), 8.17 (d, *J*=8.46 Hz, 1H), 8.60 (m, *J*=5.79, 1.88, 1.88 Hz, 1H), 8.68 (dd, *J*=4.41, 1.10 Hz, 1H), 8.82 (dd, *J*=4.78, 1.84 Hz, 1H).

Example 101

5-chloro-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-1-(3-methylbutyl)-2(1H)-quinolinone

Example 101A

5-chloro-2*H*-3,1-benzoxazine-2,4(1*H*)-dione

A solution of potassium hydroxide (1.68 g, 30 mmol) and 2-amino-6-chlorobenzoic acid (3.43 g, 20 mmol) in water (25 mL) at 0 °C was treated dropwise with 20% phosgene in toluene (16.8 mL, 32 mmol) resulting in a precipitate. The mixture was stirred for 1 hour and

the solid was collected by filtration, washed with water and dried to give the title compound (3.6 g, 91%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.11 (d, *J*=7.35 Hz, 1H), 7.31 (d, *J*=6.99 Hz, 1H), 7.66 (t, *J*=8.09 Hz, 1H), 11.83 (s, 1H).

Example 101B

5-chloro-1-(3-methylbutyl)-2*H*-3,1-benzoxazine-2,4(1*H*)-dione

The title compound was prepared according to the procedure of Example 1B substituting 1-bromo-3-methylbutane for n-butyl bromide and substituting the product of Example 101A for the product of Example 1A (0.610 g, 45%). MS (DCI) m/z 285 $(M+NH_4)^+$.

Example 101C

ethyl 5-chloro-4-hydroxy-1-(3-methylbutyl)-2-oxo-1,2-dihydroquinoline-3-carboxylate

The title compound was prepared according to the procedure of Example 89A substituting the product of Example 101B for the product of Example 1B (0.600 g, 80%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.96 (d, *J*=6.62 Hz, 6H), 1.32 (t, *J*=7.17 Hz, 3H), 1.44 (m, 2H), 1.70 (m, *J*=13.24, 6.62 Hz, 1H), 4.18 (m, 2H), 4.35 (q, *J*=6.99 Hz, 2H), 7.35 (d, *J*=6.99 1H), 7.48 (d, *J*=8.09 Hz, 1H), 7.67 (m, 1H), 13.88 (s, 1H).

Example 101D

N-[2-(aminosulfonyl)pyridin-3-yl]-5-chloro-4-hydroxy-1-(3-methylbutyl)-2-oxo-1,2-dihydroquinoline-3-carboxamide

The product of Example 101C (0.170 g, 0.50 mmol) was reacted with the product of Example 98A (0.086 g, 0.50 mmol) in toluene (6 mL) at reflux for 16 hours. The reaction was cooled and the resulting precipitate was collected by filtration and dried to give the title compound (0.200 g, 86%). MS (DCI) m/z 465 $(M+H)^+$. 1 ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.99 (d, *J*=6.62 Hz, 6H), 1.51 (m, 2H), 1.76 (m, 1H), 4.32 (m, 2H), 7.45 (d, *J*=7.35 Hz, 1H), 7.61 (d, *J*=8.82 Hz, 1H), 7.71 (s, 2H), 7.77 (m, 2H), 8.45 (dd, *J*=8.46, 1.47 Hz, 1H), 8.53 (dd, *J*=4.60, 1.29 Hz, 1H), 12.84 (s, 1H), 17.22 (s, 1H).

Example 101E

5-chloro-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-1-(3-methylbutyl)-2(1H)-quinolinone

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 101D for the product of Example 84C (0.200 g, 98%). MS (ESI-) m/z 445 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.98 (d, *J*=6.62 Hz, 6H),

1.45 (m, 2H), 1.71 (m, 1H), 4.11 (m, 2H), 7.08 (d, *J*=7.35 Hz, 1H), 7.23 (d, *J*=8.09 Hz, 1H), 7.43 (t, *J*=8.27 Hz, 1H), 7.57 (dd, *J*=8.46, 4.41 Hz, 1H), 7.78 (d, *J*=8.09 Hz, 1H), 8.45 (d, *J*=4.41 Hz, 1H), 15.77 (s, 1H).

Example 102

1-benzyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-5-methyl-2(1H)-quinolinone

Example 102A

1-Benzyl-(4-methyl)benzo[2,3-d][1,3]oxazine-2,4-dione

The title compound was prepared according to the procedure of Example 1B substituting benzyl bromide for n-butyl bromide and substituting (4-methyl)benzo[2,3-d][1,3]oxazine-2,4-dione for the product of Example 1A (0.67 g, 60%). MS (DCI+) m/z 268 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.66 (s, 3H), 5.28 (s, 2H), 7.07 (d, *J*=8.48 Hz, 1H), 7.14 (d, *J*=7.80 Hz, 1H), 7.33 (m, 5H), 7.57 (t, *J*=7.46 Hz, 1H).

Example 102B

ethyl 1-benzyl-4-hydroxy-5-methyl-2-oxo-1,2-dihydroquinoline-3-carboxylate

The title compound was prepared according to the procedure of Example 84A substituting the product of Example 102A for the product of Example 15A (0.71 g, 89%). MS (DCI+) m/z 338 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.33 (t, *J*=7.17 Hz, 3H), 2.77 (s, 3H), 4.39 (q, *J*=7.23 Hz, 2H), 5.47 (s, 2H), 7.05 (d, *J*=7.35 Hz, 1H), 7.20 (m, 4H), 7.31 (m, 2H), 7.47 (t, *J*=8.09 Hz, 1H), 14.43 (s, 1H).

Example 102C

N-[2-(aminosulfonyl)pyridin-3-yl]-1-benzyl-4-hydroxy-5-methyl-2-oxo-1,2-dihydroquinoline-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting the product of Example 102B for the product of Example 84B and substituting the product of Example 98A for 2-amino-5-bromobenzenesulfonamide (0.163 g, 41%). MS (ESI+) m/z 465 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.82 (s, 3H), 5.59 (s, 2H), 7.15 (d, *J*=7.35 Hz, 1H), 7.24 (m, 3H), 7.33 (m, 3H), 7.56 (t, *J*=7.91 Hz, 1H), 7.72 (m, 3H), 8.51 (m, 1H), 8.53 (s, 1H), 12.93 (s, 1H), 17.16 (m, 1H).

Example 102D

1-benzyl-3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-5-methyl-2(1H)-quinolinone

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 102C for the product of Example 84C (0.064 g, 41%). MS (ESI+) m/z 447 $(M+H)^+$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. MS (ESI-) m/z 445 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.81 (s, 3H), 5.37 (dd, *J*=6.07, 2.02 Hz, 2H), 6.80 (d, *J*=7.35 Hz, 1H), 6.95 (d, *J*=8.09 Hz, 1H), 7.20 (m, 4H), 7.29 (m, 2H), 7.57 (dd, *J*=8.46, 4.41 Hz, 1H), 7.75 (dd, *J*=8.46, 1.47 Hz, 1H), 8.44 (dd, *J*=4.41, 1.47 Hz, 1H), 16.29 (s, 1H).

Example 103

3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-1-[(2-methyl-1,3-thiazol-5-yl)methyl]-2(1H)-quinolinone

Example 103A

1-[(2-methyl-1,3-thiazol-5-yl)methyl]-2*H*-3,1-benzoxazine-2,4(1*H*)-dione

The title compound was prepared according to the procedure of Example 1B substituting isatoic anhydride for the product of Example 1A and 2-methyl-5-chloromethylthiazole for n-butyl bromide to give (0.410 g, 73%).

Example 103B

ethyl 1-[(2-methyl-1,3-thiazol-5-yl)methyl]-2,4-dioxo-1,2,3,4-tetrahydroquinoline-3-carboxylate

The title compound was prepared according to the procedure of Example 84A substituting the product of Example 103A for the product of Example 15B (0.132 g, 25%). MS (ESI-) m/z 343 $(M-H)^-$; ^{1}H NMR (300 MHz, $CDCl_3$) δ. 1.49 (t, *J*=6.99 Hz, 3H), 2.61 (s, 3H), 4.53 (q, *J*=7.23 Hz, 2H), 5.54 (s, 2H), 7.27 (t, *J*=8.09 Hz, 1H), 7.41 (d, *J*=8.46 Hz, 1H), 7.62 (s, 1H), 7.67 (m, 1H), 8.21 (dd, *J*=8.09, 1.47 Hz, 1H), 14.32 (s, 1H).

Example 103C

N-[2-(aminosulfonyl)pyridin-3-yl]-1-[(2-methyl-1,3-thiazol-5-yl)methyl]-2,4-dioxo-1,2,3,4-tetrahydroquinoline-3-carboxamide

The title compound was prepared as described in the procedure of Example 84C substituting the product of Example 99A for the product of Example 84B and substituting 3-amino-pyridine-2-sulfonamide for 2-amino-5-bromobenzenesulfonamide (0.148 g, 79%). MS (APCI) m/z 472 $(M+H)^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ. 2.55 (s, 3H), 5.69 (s, 2H), 7.25 (m, 1H), 7.35 (s, 1H), 7.42 (t, *J*=6.62 Hz, 1H), 7.81 (m, 4H), 8.17 (d, *J*=7.72 Hz, 1H), 8.52 (d, *J*=2.57 Hz, 1H), 8.54 (s, 1H), 12.67 (s, 1H), 16.28 (s, 1H).

Example 103D

3-(1,1-dioxido-4H-pyrido[3,2-e][1,2,4]thiadiazin-3-yl)-4-hydroxy-1-[(2-methyl-1,3-thiazol-5-yl)methyl]-2(1H)-quinolinone

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 103C for the product of Example 84C (0.033 g, 68%). MS (APCI) m/z 454 $(M+H)^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 2.56 (s, 3H), 5.74 (s, 2H), 7.48 (t, J=6.80 Hz, 1H), 7.82 (s, 1H), 7.88 (m, 4H), 8.24 (m, 2H), 8.71 (dd, J=4.41, 1.47 Hz, 1H), 14.01 (s, 1H).

Example 104

1-benzyl-4-hydroxy-3-(7-methyl-1,1-dioxido-4H-pyrido[2,3-e][1,2,4]thiadiazin-3-yl)-2(1H)-quinolinone

Example 104A

(2-Amino-5-methylpyrid-3-yl)sulfonyl chloride

(2-Amino-5-methylpyrid-3-yl)sulfonyl chloride was prepared from 2-amino-5-picoline by the method described by Weller, H.N. in US 5,378,704. ^1H NMR (300 MHz, DMSO-d_6) δ 2.20 (s, 3H), 7.70 (br. s., 2H), 7.85 (d, J=5.52 Hz, 1H), 8.07 (d, J=2.21 Hz, 1H).

Example 104B

2-amino-5-methylpyridine-3-sulfonamide

The product of Example 104A was reacted with concentrated ammonium hydroxide at ambient temperature overnight. The reaction mixture was concentrated to give the title compound as a light yellow solid in quantitative yield. MS (DCI/NH_3) m/z 188 $(M+H)^+$. ^1H NMR (300 MHz, DMSO-d_6) δ 2.17 (m, 3H), 6.28 (s, 2H), 7.43 (s, 2H), 7.70 (d, J=1.84 Hz, 1H), 8.00 (d, J=2.21 Hz, 1H).

Example 104C

N-[3-(aminosulfonyl)-5-methylpyridin-2-yl]-1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinoline-3-carboxamide

The title compound was prepared according to the procedure of Example 84C substituting product of Example 104B for 2-amino-5-bromobenzenesulfonamide.

Example 104D

1-benzyl-4-hydroxy-3-(7-methyl-1,1-dioxido-4H-pyrido[2,3-e][1,2,4]thiadiazin-3-yl)-2(1H)-

quinolinone

The title compound was prepared according to the procedure of Example 84D substituting the product of Example 104C for the product of Example 84C (0.20 g, 35%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.32 (m, 3H), 5.45 (s, 2H), 5.97 (s, 1H), 7.22 (m, 9H), 7.50 (m, 1H), 7.91 (dd, *J*=7.91, 1.65 Hz, 1H), 11.50 (m, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.37 (m, 3H), 5.39 (m, 2H), 7.07 (m, 1H), 7.24 (m, 6H), 7.39 (m, 1H), 7.94 (d, *J*=1.47 Hz, 1H), 8.13 (dd, *J*=7.91, 1.65 Hz, 1H), 8.43 (d, *J*=1.84 Hz, 1H), 16.49 (m, 1H)

Example 105

1-butyl-4-hydroxy-3-(7-methyl-1,1-dioxido-4H-pyrido[2,3-e][1,2,4]thiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

Example 105A

ethyl 3-{[3-(aminosulfonyl)-5-methylpyridin-2-yl]amino}-3-oxopropanoate

The product of Example 104B (1.0 g, 0.0053 mol) in 10 mL of THF containing 5 mL of pyridine was treated with ethyl 3-chloro-3-oxopropionate (0.97 g, 0.0064 mol) at ambient temperature for several hours. The reaction mixture was concentrated to half its original volume and then diluted with water. The resulting precipitate was collected by filtration and washed with water and dried under vacuum to give the title compound as an off white solid (1.19 g, 75% yield). MS (ESI) m/z 300 $(M-H)^-$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.19 (t, *J*=7.17 Hz, 3H), 2.35 (s, 3H), 3.65 (s, 2H), 4.11 (q, *J*=7.23 Hz, 2H), 7.60 (s, 2H), 8.06 (d, *J*=1.47 Hz, 1H), 8.41 (d, *J*=1.84 Hz, 1H), 9.79 (s, 1H).

Example 105C

ethyl (7-methyl-1,1-dioxido-4*H*-pyrido[2,3-*e*][1,2,4]thiadiazin-3-yl)acetate

The product of Example 105A (0.363 g, 0.0012 mol) in 20 mL of ethanol was reacted with sodium carbonate (0.350 g, 0.0033 mol). The reaction mixture was heated at reflux for 2 hours. After cooling, the reaction mixture was diluted with dichloromethane, filtered to remove the excess sodium carbonate, and concentrated. The residue was purified chromatography on silica gel with ethyl acetate in hexanes (1:1) followed by 4% methanol in dichloromethane as the mobile phase to give the title compound as a white solid (0.296 g, 87% yield). MS (ESI) m/z 282 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.21 (t, *J*=6.99 Hz, 3H), 2.40 (s, 3H), 3.73 (s, 2H), 4.15 (q, *J*=7.11 Hz, 2H), 8.20 (s, 1H), 8.58 (d, *J*=1.84 Hz, 1H), 12.79 (s, 1H).

Example 105D

1-butyl-4-hydroxy-3-(7-methyl-1,1-dioxido-4H-pyrido[2,3-e][1,2,4]thiadiazin-3-yl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 105C for the product of Example 1C (0.065 g, 58% yield). ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.94 (t, *J*=7.35 Hz, 3H), 1.40 (m, 2H), 1.67 (m, 2H), 2.44 (m, 3H), 4.46 (dd, *J*=7.91, 7.17 Hz, 2H), 7.48 (dd, *J*=8.09, 4.78 Hz, 1H), 8.29 (s, 1H), 8.56 (dd, *J*=7.91, 1.65 Hz, 1H), 8.64 (d, *J*=1.47 Hz, 1H), 8.87 (d, *J*=5.52 Hz, 1H). The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.93 (t, *J*=7.35 Hz, 3H), 1.34 (m, 2H), 1.58 (m, 2H), 2.36 (s, 3H), 4.26 (d, *J*=7.72 Hz, 1H), 4.29 (d, *J*=6.99 Hz, 1H), 7.13 (dd, *J*=7.72, 4.78 Hz, 1H), 7.95 (s, 1H), 8.37 (dd, *J*=7.72, 2.21 Hz, 1H), 8.42 (d, *J*=1.84 Hz, 1H), 8.53 (dd, *J*=4.60, 2.02 Hz, 1H), 16.11 (s, 1H).

Example 106

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-thienylmethyl)-1,8-naphthyridin-2(1H)-one

Example 106A

1-(thien-2-ylmethyl)-2*H*-pyrido[2,3-*d*][1,3]oxazine-2,4(1*H*)-dione

The title compound was prepared according to the procedure of Example 1B substituting 2-(bromomethyl)-thiophene for n-butyl bromide (0.165 g, 51%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.48 (s, 2H), 6.97 (dd, *J*=5.15, 3.31 Hz, 1H), 7.21 (d, *J*=3.31 Hz, 1H), 7.43 (m, 2H), 8.41 (dd, *J*=7.72, 1.84 Hz, 1H), 8.83 (dd, *J*=5.15, 1.84 Hz, 1H).

Example 106B

3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1-(2-thienylmethyl)-1,8-naphthyridin-2(1H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 106A for the product of Example 1B (0.162 g, 60%). MS (ESI-) m/z 437 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.64 (s, 2H), 6.90 (m, *J*=5.15, 3.68 Hz, 1H), 7.11 (m, *J*=3.49, 0.92 Hz, 1H), 7.18 (dd, *J*=7.72, 4.78 Hz, 1H), 7.29 (m, 3H), 7.56 (m, 1H), 7.67 (dd, *J*=7.72, 1.10 Hz, 1H), 8.39 (dd, *J*=7.72, 2.21 Hz, 1H), 8.57 (dd, *J*=4.78, 1.84 Hz, 1H), 15.80 (s, 1H).

Example 107

1-(benzyloxy)-3-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-

2(1H)-one

Example 107A

ethyl 2-[(benzyloxy)amino]nicotinate

2-Chloro-nicotinic acid ethyl ester (4.55 g, 24.6 mmol), O-benzylhydroxyamine hydrochloride (7.85 g, 49.2 mmol) and N,N-diisopropylethylamine (6.36 g, 49.2 mmol) in 10 mL 1,4-dioxane were reacted in a sealed tube at 120 °C for 48 hours. The reaction mixture was partitioned between ethyl acetate and 5% aqueous sodium bicarbonate. The aqueous layer was re-extracted with ethyl acetate (2 x 50 mL). The organic layers were combined and dried over sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography on silica gel eluting with hexane and ethyl acetate (9:1) to provide the title compound (3.5 g, 53%). MS (DCI) m/z 273 $(M+H)^+$.

Example 107B

ethyl 2-[(benzyloxy)(3-ethoxy-3-oxopropanoyl)amino]nicotinate

A solution of the product of Example 107a (1.2 g, 4.4 mmol) and triethylamine (0.49 g, 4.8 mmol) in dichloromethane (25 mL) was treated dropwise with ethyl chloromalonate (0.73 g, 4.8 mmol), stirred for 2 hr and partitioned between ethyl acetate and water and the layers were separated. The ethyl acetate layer was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel eluting with hexane and ethyl acetate (3:1) to provide the title compound (1.1 g, 65%). MS (DCI) m/z 387 $(M+H)^+$.

Example 107C

ethyl 1-(benzyloxy)-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxylate

A solution of the product of Example 107b (0.386 g, 1.0 mmol) in ethanol (5 mL) was treated with 21% sodium ethoxide in ethanol (0.324 g, 1.0 mmol), stirred for 30 minutes and partitioned between ethyl acetate and 5% aqueous HCl and the layers were separated. The ethyl acetate layer was washed with brine, dried (Na_2SO_4), and concentrated to provide the title compound (0.28 g, 82%). MS (DCI) m/z 341$(M+H)^+$.

Example 107D

N-[2-(aminosulfonyl)phenyl]-1-(benzyloxy)-4-hydroxy-2-oxo-1,2-dihydro-1,8-naphthyridine-3-carboxamide

A mixture of the product of Example 107c (340 mg, 0.82 mmol) and 2-aminobenzenesulfonamide (141 mg, 0.82 mmol) in toluene (10 mL) was refluxed for 16 hours, cooled, and the resulting precipitate was collected by filtration and dried to give the title compound (340 mg, 89%). MS (DCI) m/z 467 $(M+H)^+$.

Example 107E

1-(benzyloxy)-3-(1,1-dioxido-4*H*-1,2,4-benzothiadiazin-3-yl)-4-hydroxy-1,8-naphthyridin-

2(1*H*)-one

The title compound was prepared according to the procedure of Example 84d substituting the product of Example 107d for the product of Example 84c to give the title compound (0.082 g, 87%). MS (ESI-) m/z 447 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1d. 1H NMR (300 MHz, DMSO-d6) δ 5.12 (s, 2 H) 7.22 (dd, *J*=7.72, 4.78 Hz, 1 H) 7.30 (m, 2 H) 7.44 (m, 3 H) 7.57 (m, 1 H) 7.70 (m, 3 H) 8.41 (dd, *J*=7.72, 1.84 Hz, 1 H) 8.61 (dd, *J*=4.78, 1.84 Hz, 1 H) 15.70 (s, 1 H).

Example 108

6-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-8-(2-ethylbutyl)-5-hydroxy-2-(methylsulfanyl)pyrido[2,3-d]pyrimidin-7(8H)-one

Example 108A

methyl 4-[(2-ethylbutyl)amino]-2-(methylthio)pyrimidine-5-carboxylate

Ethyl 4-chloro-2-methylthio-5-pyrimidinecarboxylate (0.40 g, 1.72 mmol) was reacted with 1-amino-2-ethyl butane (0.175 g, 1.72 mmol) and triethylamine (0.60 mL, 4.32 mmol) at ambient temperature for 18 hours. The reaction was partitioned between water and dichloromethane. The organic layer was dried over sodium sulfate, filtered, and the concentrated to give the title compound (0.50 g, 98%).

Example 108B

4-[(2-ethylbutyl)amino]-2-(methylthio)pyrimidine-5-carboxylic acid

The product of Example 108A (0.50 g, 1.68 mmol)) in water and ethanol (1:2) was reacted with sodium hydroxide (0.22 g, 5.50 mmol) at ambient temperature for 3 hours. The reaction was concentrated under vacuum to remove the ethanol and neutralized with aqueous hydrochloric acid (1 M). The resulting precipitate was collected by filtration and dried to yield the title compound (0.41 g, 91%). MS (DCI/NH_3) m/z 270 $(M+H)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.88 (t, *J*=7.54 Hz, 6H), 1.31 (dt, *J*=14.25, 7.03 Hz, 4H), 1.53 (m, 1H), 2.47 (s, 3H), 3.46 (t, *J*=6.07 Hz, 2H), 8.50 (s, 1H), 13.22 (s, 1H).

Example 108C

1-(2-ethylbutyl)-7-(methylthio)-2*H*-pyrimido[4,5-*d*][1,3]oxazine-2,4(1*H*)-dione

The product of Example 108B (0.41 g, 1.52 mmol) was reacted with ethyl chloroformate (0.445 mL, 4.65 mmol) and pyridine (0.405 mL, 5.56 mmol) in toluene (8 ML) at 90°C for 24 hours. The reaction was concentrated under vacuum. The residue was extracted with ethyl acetate and filtered. Concentration of the filtrate gave the title

compound (0.394 g, 88%).

Example 108D

6-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-8-(2-ethylbutyl)-5-hydroxy-2-(methylsulfanyl)pyrido[2,3-d]pyrimidin-7(8H)-one

The title compound was prepared according to the procedure of Example 1D substituting the product of Example 108C for the product of Example 1B (0.153 g, 24%). MS (ESI-) m/z 472 $(M-H)^-$. The sodium salt of the title compound was prepared according to the procedure of Example 1D. ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.87 (t, *J*=7.54 Hz, 6H), 1.28 (m, 4H), 1.87 (ddd, *J*=13.05, 6.80, 6.62 Hz, 1H), 2.56 (s, 3H), 4.15 (d, *J*=7.35 Hz, 2H), 7.26 (d, *J*=8.46 Hz, 1H), 7.31 (m, 1H), 7.56 (ddd, *J*=8.27, 7.17, 1.47 Hz, 1H), 7.67 (dd, *J*=7.72, 1.47 Hz, 1H), 8.89 (s, 1H), 15.52 (s, 1H).

Example 109

6-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-8-(2-ethylbutyl)-5-hydroxypyrido[2,3-d]pyrimidin-7(8H)-one

The product of Example 108D (0.15 g, 0.30 mmol) was reacted with an excess of Raney nickel (slurry in water, 2 mL) in ethanol (5 mL) and heated at 60 °C for 1 hour. The mixture was filtered through celite, rinsed with ethanol, and the filtrate concentrated under vacuum to yield the title compound. MS (ESI-) m/z 448 $(M-H)^-$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.86 (t, *J*=7.35 Hz, 6H), 1.28 (m, 4H), 1.87 (m, 1H), 4.18 (d, *J*=7.35 Hz, 2H), 7.30 (m, 2H), 7.57 (ddd, *J*=8.27, 7.17, 1.47 Hz, 1H), 7.68 (dd, *J*=7.91, 1.29 Hz, 1H), 8.94 (s, 1H), 9.09 (s, 1H), 15.43 (s, 1H).

Example 110

4-benzyl-6-(1,1-dioxido-4H-1,2,4-benzothiadiazin-3-yl)-7-hydroxythieno[3,2-b]pyridin-5(4H)-one

Example 110A

2*H*-thieno[3,2-*d*][1,3]oxazine-2,4(1*H*)-dione

The title compound was prepared according to the procedure of Fabis, and co-workers as described in *Tetrahedron*, 1998, 54, 10789-10800. MS (DCI/NH_3) m/z 186.9 $(M+NH_4)^+$; ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.95 (d, J=6 Hz, 1 H) 8.25 (d, J=6 Hz, 1 H) 12.22 (brs, 1 H).

Example 110B

1-benzyl-2*H*-thieno[3,2-*d*][1,3]oxazine-2,4(1*H*)-dione

The product of Example 110A (0.137 g, 0.81mmol) was reacted with benzyl bromide